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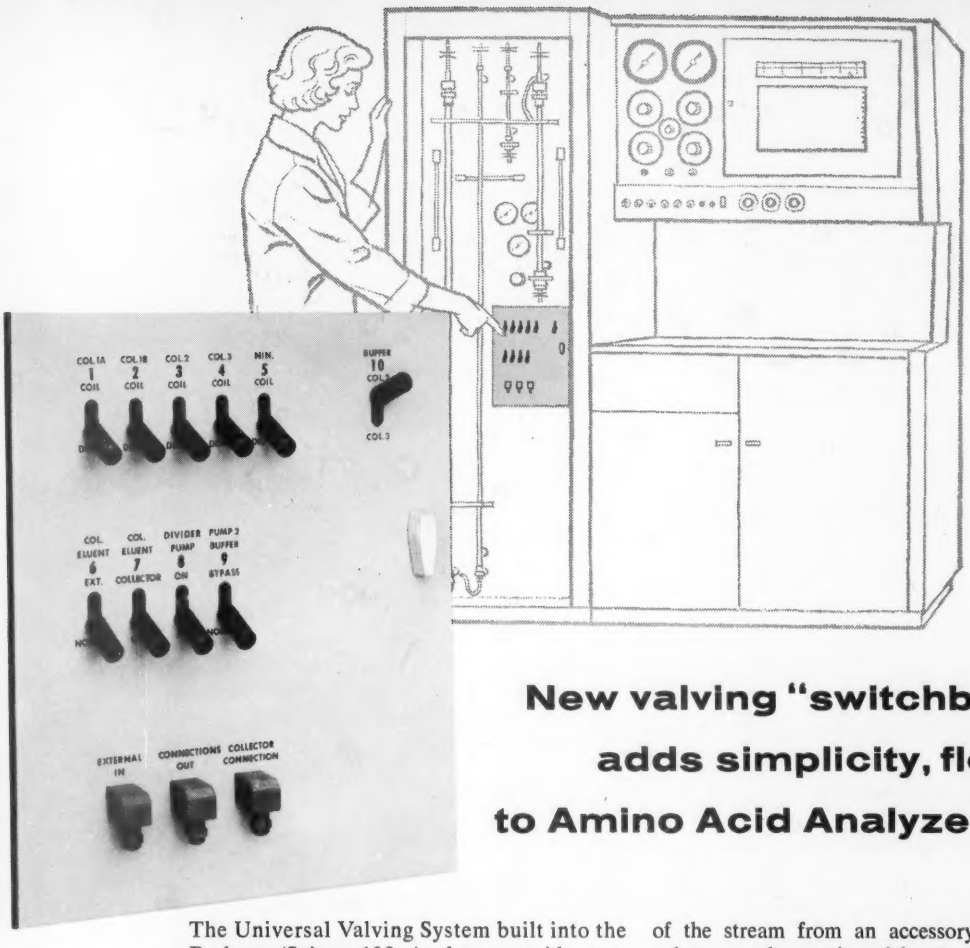

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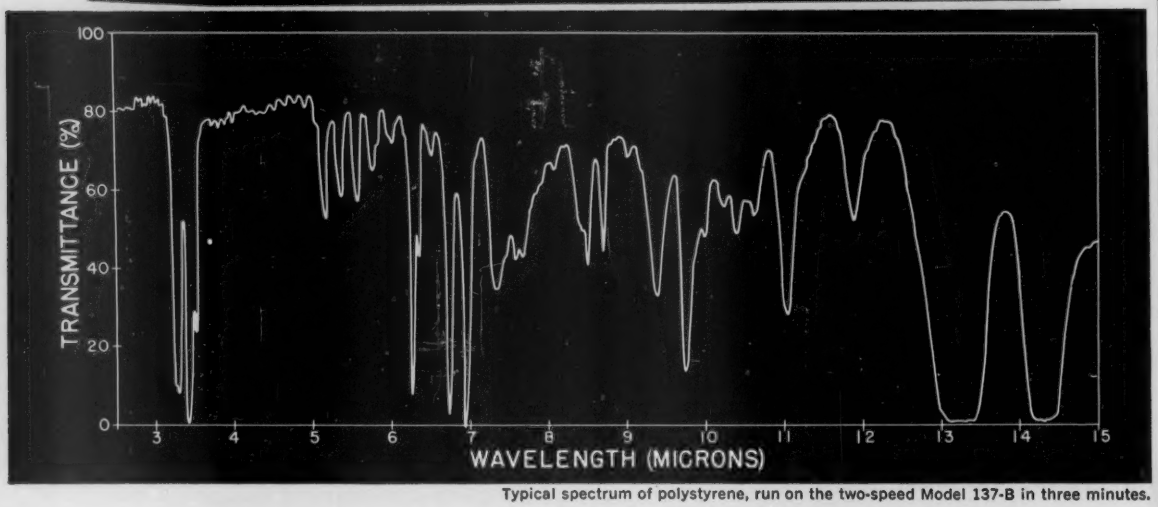

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A female *Lampsilis ovata ventricosa* (Barnes). This fresh-water mussel is one of a family having glochidia or young that are parasitic on the gills of fishes. The females of this group, during the breeding season, develop lures, such as the fish-like projections of the edge of the mantle shown here. These projections attract fish to the vicinity of the mussel, thereby assuring transfer of the young larva to the host. [J. H. Welsh, Biological Laboratories, Harvard University]

*American Journal of Clinical Pathology Vol. 33. No. 2. February 1960, pp 144-151 "Application of Refrigerated Microtome in Surgical Pathology" by Bernard Klionsky, M.D. and Othello D. Smith, M.D.

The Journal of Histochemistry and Cytochemistry Vol. 8, No. 5. September, 1960, pp 310 "A Frozen Section Freeze Substitutions Technique and an Improved Cryostat" by Jeffrey P. Chang and Samuel H. Hori.

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The Company They Keep

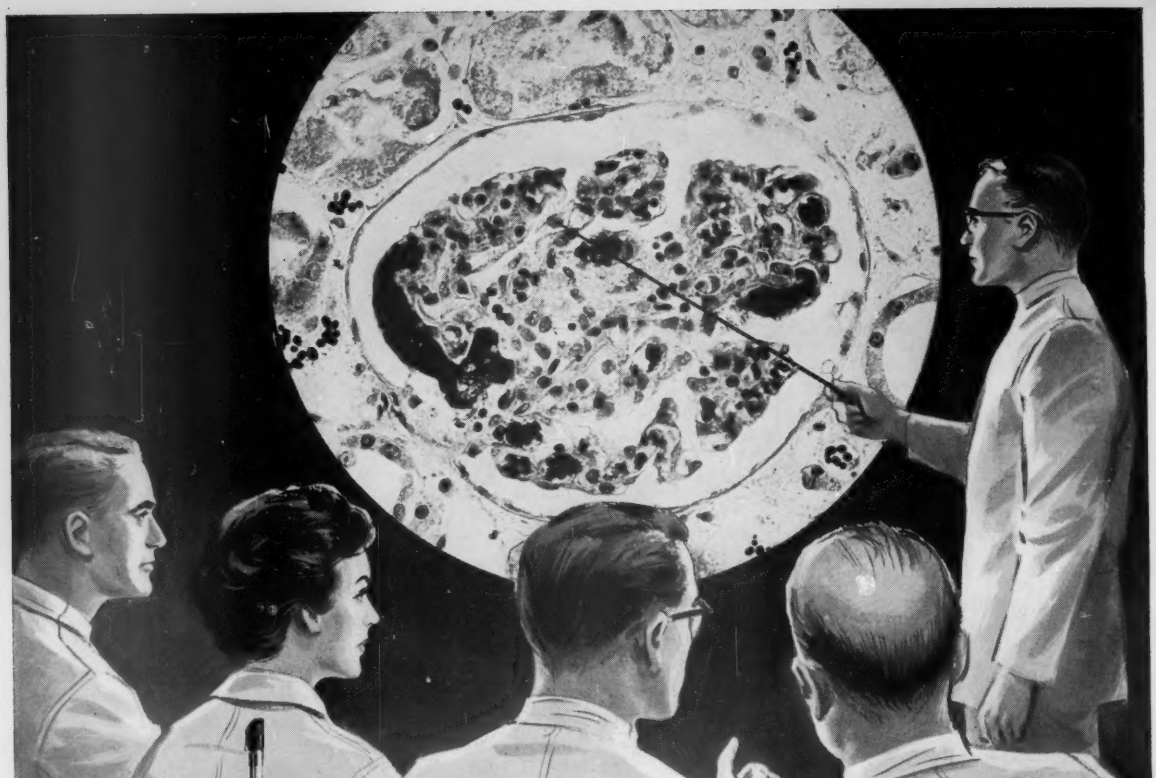
One of the tasks of the Federal Trade Commission, according to the Encyclopaedia Britannica, is to order business organizations to stop using deceptive advertising when such organizations are found to be so engaged. A few weeks ago Encyclopaedia Britannica, Inc., was ordered by the Federal Trade Commission to stop using advertising that misrepresents its regular prices as reduced prices available for a limited time only. Besides the familiar 24-volume Encyclopaedia, the company sells such things as a book case, an atlas, a reference service, and the Britannica book of the year. Sales are made directly to the public through the publisher's 2500 or so salesmen, with advertising in national magazines backing up the sales force.

Some of the company's sales practices are ingenious. The FTC shows, for example, how the prospective customer, once he has gained the impression that he is being offered the Encyclopaedia and accessories at reduced prices, is led to believe that the purported reduced prices are good only for a limited time. This is done by two kinds of statements, each being true enough if regarded separately.

The first kind of statement, which appears in written material, says such things as "This offer is necessarily subject to withdrawal without notice." Such a statement, as the company pointed out at the hearings, is not untrue. The offer certainly *could* be withdrawn, although, as a matter of fact, with the exception of a version of the Encyclopaedia bound in something called "Blue Levantex," there has been no change in prices since 1949. The second kind of statement is made orally by the salesmen. Upon conclusion of the sales presentation, if the prospective customer wants to think things over, the salesman will say that the prospect had better make his mind up right away, for the salesman will not return. And again, as the company also argued, the statement is true enough. The threat is not empty, for, in fact, salesmen generally do not call again.

But the two kinds of statements taken together, according to the FTC, create an illusion. The refusal of the salesman to return, viewed against the warning that the offer is subject to withdrawal—and also viewed against the impression, created by other means, that a reduced price is being offered—leads the prospect to believe that the salesman's refusal means the withdrawal of an opportunity to obtain reduced prices. Interestingly enough, although the threat not to return is not empty, carrying it out involves no loss to the company. Experience has shown that when a sale is not completed on the first call, the salesman will do better trying his luck on a new prospect rather than going back to the old one.

In volume I of the Britannica, after the dedications to John Fitzgerald Kennedy and Queen Elizabeth II, there are acknowledgements to the many persons whose "cordial cooperation," as the editors put it, makes this enterprise possible. These many persons are the professors of the Universities of Chicago, Oxford, Cambridge, and London who provided editorial advice, and the thousands of authorities in different fields who wrote the actual articles. Perhaps, then, the FTC should not be the only group reviewing the business practices of Encyclopaedia Britannica, Inc. A committee of these authorities might also have some thoughts on the methods by which their efforts are being sold. Should these methods not earn the committee's approval, it might advise contributors to make their cooperation a bit less cordial.—J.T.



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CURRENT PROBLEMS IN RESEARCH

Electrical Resistivity at Low Temperatures

The pressure dependence of the electrical resistance of metals gives some clues about their Fermi surfaces.

J. S. Dugdale

During this century there have been many investigations of the dependence of electrical resistivity of metals on temperature and pressure (*1*, *2*). Broadly speaking, however, most of the temperature measurements have been made at atmospheric pressure, and most of the pressure measurements have been made at temperatures around room temperature. I would like here to describe some experiments which combine the two kinds of measurements and which are designed to find out how resistivity depends on pressure at *low* temperatures.

Why do we want this information? I shall first try to answer this question by contrasting the changes brought about by variations of temperature with those brought about by variations of pressure. We may think of a solid metal as consisting of a lattice of positive ions agitated by thermal vibrations and of an interpenetrating gas of conduction electrons. For many purposes we may discuss the metal in terms of its energy levels—for example, the energy levels associated with the normal modes of vibration of the lattice or the allowed kinetic energy levels of the conduction electrons. In general, if the volume does not change, these energy levels do not change, and an alteration of the temperature simply alters the *distribution* of the electrons or lattice vibrations among these levels. But if the volume changes, then the levels themselves also change. Thus, changing the temperature at fixed volume acts as a method (albeit a rather gross one) of exploring how these levels are distributed; altering the volume is a means of changing them. A combination of the two methods therefore enables us both to change the levels and to investigate their properties after the change.

Having emphasized the different roles of temperature and pressure changes, I would now like to show that in certain ways they are closely related. It is a fact of experience that the thermal expansion coefficient of most substances is positive. Consequently, from the thermodynamic identity expressed in the equation:

$$\left(\frac{\partial V}{\partial T}\right)_p = -\left(\frac{\partial S}{\partial p}\right)_T \qquad (1)$$

it follows that the entropy of such substances falls when they are isothermally compressed. But now it is well-known from thermodynamics that at constant pressure the entropy of a substance also falls when its temperature is lowered. We therefore see that in this respect an increase in pressure is similar to a decrease in temperature. Indeed, so attractive is this idea that G. N. Lewis (*3*) wished to use it as a basis for extending the third law of thermodynamics. His tentative statement of such an extension was as follows: "At all temperatures the entropy of a pure crystal is zero at infinite pressure." The proposal was never in fact developed, presumably because the extrapolation to infinite pressure cannot usefully be made; whatever the formal similarity between increasing pressure and decreasing temperature, their actual physical effects are ultimately quite different (*4*). For more restricted purposes, however, this similarity is quite valid and very useful, as I now hope to show.

The equilibrium lattice properties of many metals can be discussed in terms of a reduced temperature $\tau = T/\theta$, where T is the actual temperature and θ is the characteristic lattice temperature of the metal (for example, the Debye temperature). θ, which ideally is independent of T, is related to the characteristic frequency of the lattice, and if the lattice is compressed its characteristic frequency, and hence θ, increases. Thus the reduced temperature may be decreased either by reducing the actual temperature or by increasing the pressure. This suggests that pressure coefficients and temperature coefficients must be related. Take, as an example, the lattice entropy S, which depends only on T/θ. Thus

$$\left(\frac{\partial S}{\partial T}\right)_V = \frac{S'}{\theta} \qquad \left(S' \equiv \frac{dS}{d\tau}\right)$$

$$\left(\frac{\partial S}{\partial V}\right)_T = -\frac{S'}{\theta} \cdot \frac{T}{V} \cdot \frac{d \ln \theta}{d \ln V}$$

Therefore

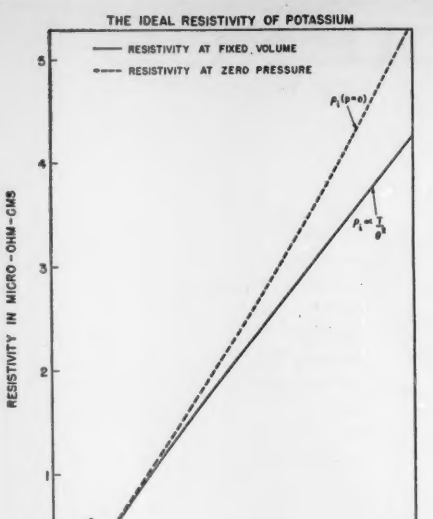
$$\left(\frac{d \ln S}{d \ln V}\right)_T = \gamma \left(\frac{d \ln S}{d \ln T}\right)_V \qquad (2)$$

Here I have introduced the parameter γ (which equals $-d \ln \theta / d \ln V$), called the Grüneisen parameter. We thus see that the volume coefficient of entropy is related to the temperature coefficient of entropy by the parameter γ. In fact, a thermodynamic transformation of this equation leads to Grüneisen's law of thermal expansion:

$$\frac{1}{V}\left(\frac{\partial V}{\partial T}\right)_p = \frac{\gamma \beta C_V}{V} \qquad (3)$$

where C_V is the specific heat at constant volume, β is the compressibility, and $(1/V)[(\partial V/\partial T)_p]$ is the thermal expansion coefficient. This relationship then affords a means for determining γ (which measures the change of θ with

The author is on the staff of the National Research Council, Ottawa, Canada, in the Division of Pure Physics.



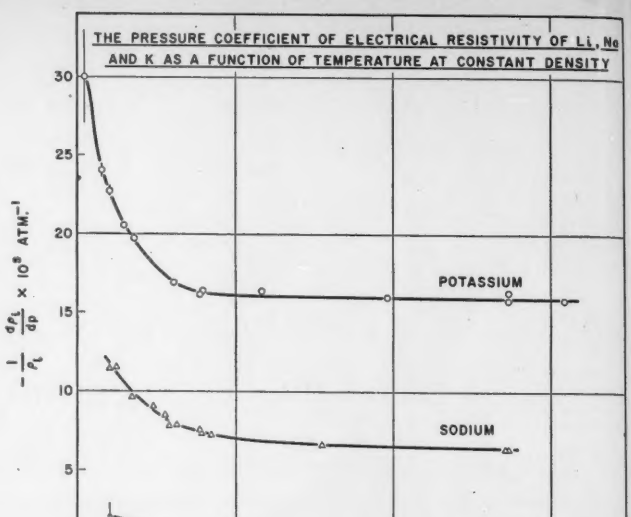


Fig. 1 (left). The electrical resistivity of potassium as a function of temperature. The solid line shows the resistivity at a fixed volume (that at 0°K under zero pressure); this is the quantity which is most convenient for direct comparison with theory. Fig. 2 (right). The pressure coefficient of electrical resistivity of lithium, sodium, and potassium as a function of temperature at constant density (*13*).

volume) in terms of readily observable quantities.

Considerations of this kind can also be applied to the discussion of the pressure dependence of the electrical resistivity of metals, but first I must describe briefly how this resistivity depends on the temperature (*5*). It is convenient to distinguish between two sources of electrical resistivity: (i) a temperature-dependent part ρ_i (the ideal resistivity), due to the thermal vibrations of the lattice, which vanishes as the temperature approaches zero, and (ii) a temperature-independent part ρ_0 (the residual resistivity), which is due to chemical and physical imperfections in the lattice.

In a perfectly periodic lattice the conduction electrons can move without hindrance; that is to say, the electrical resistance of the metal is then zero. If physical imperfections or chemical impurities are introduced into the lattice, these will then upset the perfect periodicity and cause electrical resistance by scattering the electrons when they are accelerated by an electric field. If, in addition, the lattice temperature is raised so that thermal vibrations of the ions begin, these vibrations also contribute to the electrical resistance. The part of the resistance caused by the lattice vibrations may be thought of as approximately proportional to the mean square amplitude of vibration of the ions. If the mass of the ions is M, their characteristic vibrational frequency is ω, and their amplitude of vibration is x, then at a high temperature T

$$M\omega^2\overline{x^2} = kT$$

by the classical theorem of the equipartition of energy. Therefore, by introducing a characteristic temperature θ such that $\hbar\omega = k\theta$,

$$\overline{x^2} = \frac{\hbar^2}{k}\,\frac{T}{M\theta^2}$$

and the resistivity due to thermal vibrations, ρ_i, is proportional to $T/M\theta^2$. At the lowest temperatures ρ_i is no longer proportional to the mean square amplitude of the lattice vibrations because at these temperatures the lattice waves are less efficient in scattering electrons; in fact, $\rho_i \propto T^5/\theta^6$ in this temperature region. In quantum language, it is usual to discuss the scattering of electrons by lattice waves in terms of "phonons." A phonon is a quantum of lattice energy analogous to the photon in electromagnetic radiation. The total number of phonons in the lattice varies as T at high temperatures and as T^3 at low temperatures. The temperature dependence of the number of phonons largely determines the temperature dependence of the ideal resistivity. At low temperatures, however, the "momentum" of the phonons falls off and the resistivity, as indicated above, falls off as T^5—that is, more rapidly than the number of phonons. Figure 1 illustrates the temperature dependence of the electrical resistivity of a typical monovalent metal, potassium.

If the effect of pressure on the ideal electrical resistivity arises solely from the change produced in θ, we should expect that at high temperatures

$$\frac{d\ln\rho_i}{dp} = -\frac{2d\ln\theta}{dp} \qquad (4)$$

and at low temperatures

$$\frac{d\ln\rho_i}{dp} = -\frac{6d\ln\theta}{dp} \qquad (5)$$

Since θ increases with pressure, we see at once that as far as the lattice contribution is concerned the effect of pressure is to diminish the electrical resistivity (*6*). Moreover we see that the pressure coefficient of ideal resistivity at low temperatures should be three times that at high temperatures. Figure 2 shows how the pressure coefficient of resistivity of lithium, sodium, potassium, and copper varies with temperature. The temperature dependence is of the general form to be expected. Note, however, that in lithium the pressure coefficient at high temperatures is anomalous, being positive.

In more general terms, there are theoretical grounds for believing that

$$\rho_i = \frac{K}{T} f(T/\theta_R)$$

where K measures the interaction between the conduction electrons and the lattice vibrations and θ_R is a temperature characteristic of the resistive properties of the lattice (*1*). (The results I have already quoted are simply special cases of this, indicating that at high temperatures $f(T/\theta_R)$ approaches $T^2/\theta_R{}^2$, and at low temperatures, $T^6/\theta_R{}^6$.) This relationship means that the product $\rho_i T$ is a function of a reduced temperature τ equal to T/θ_R, and we may expect, by analogy with the behavior of the thermodynamic properties of the lattice, to relate the pressure coefficient of electrical resistivity at a given temperature with the temperature coefficient of electrical resistivity at that temperature. In theoretical considerations it is more logical to work in terms of volume coefficients; in these terms the relationship is as follows (*6*):

$$\frac{d \ln \rho_i}{d \ln V} = \frac{d \ln K}{d \ln V} - \frac{d \ln \theta_R}{d \ln V}\left(1 + \frac{d \ln \rho_i}{d \ln T}\right) \quad (6)$$

The term $d \ln K / d \ln V$, which depends on the properties of the conduction electrons and on the static lattice, should be effectively independent of temperature at normal and low temperatures, as is also the term $d \ln \theta_R / d \ln V$. This relationship, therefore, tells us that the volume coefficient and the temperature coefficient of the ideal resistivity are linearly related; this in turn means that $d \ln \rho_i / d \ln V$ will change with temperature only at temperatures at which $d \ln \rho_i / d \ln T$ itself changes. This conclusion explains why we must make measurements at low temperatures if we wish to find any temperature variation of the pressure dependence of electrical resistivity, since a glance at Fig. 1 shows that only at low temperatures does the temperature coefficient of resistance change significantly.

Equation 6 means that if we measure the pressure and temperature coefficients over a suitable temperature range we can determine $d \ln \theta_R / d \ln V$ and $d \ln K / d \ln V$ separately; in this way distinguishing the lattice contribution to the pressure coefficient from the contribution of the electron properties. Before comparing the experimental results with these theoretical predictions I should like to say something about the experimental methods.

Hydrostatic Pressure at Low Temperatures

The application of hydrostatic pressure at low temperatures (*7*) presents a problem because all substances become solid under pressure at these temperatures; at pressures above about 30 atmospheres there are no true fluids at the lowest temperatures. The substance which retains its fluid properties at a given pressure to the lowest temperature is helium (the He^3 isotope is very slightly, though for our purposes not significantly, better than the He^4 isotope in this respect). For that reason, and also because solid helium can be used to produce an effectively hydrostatic pressure, we have used this substance as our pressure transmitting medium (*8*, *9*). Other solids can of course be used for this purpose [Hatton (*10*) used solid hydrogen], and for some purposes the solid to be studied can act as its own pressure medium; that is to say, the metal is directly compressed in a cylinder by a piston without any intervening substance (see *11*).

In Fig. 3 is shown part of the melting curve of He^4 (*12*). Points to the right of and below this curve correspond to the fluid phase, and as long as we are using this phase the application of pressure is quite straightforward. To understand how pressures and temperatures corresponding to the solid phase are produced, we must know something of the equation of state of the solid. This information is also indicated in Fig. 3, in which it is shown how the pressure in the solid varies with temperature at various fixed volumes (*12*). It may be seen that at constant volume the pressure in the solid is not very dependent on the temperature; this is because in solid helium most of the pressure arises from the vigorous zero-point motion of the helium atoms and is thus independent of the temperature (incidentally, it is this strong zero-point motion which makes liquid helium the stable phase at 0°K at normal pressures).

Our technique of applying high pressures in the solid state can be described as a constant-volume method. The pressure is first applied at such a temperature that the helium is still just fluid—that is, at a temperature close to, but to the right of, the melting curve shown in Fig. 3. The high-pressure bomb is then closed off so that the helium is kept effectively at constant volume, and it is then cooled to the required low temperature. In this process, in which the helium becomes solid, about one-quarter of the applied pressure is lost. However, the pressure existing in the bomb in the final state can be deduced from a knowledge of the initial density (which is also of course the final density) and the final temperature. Our measurements have

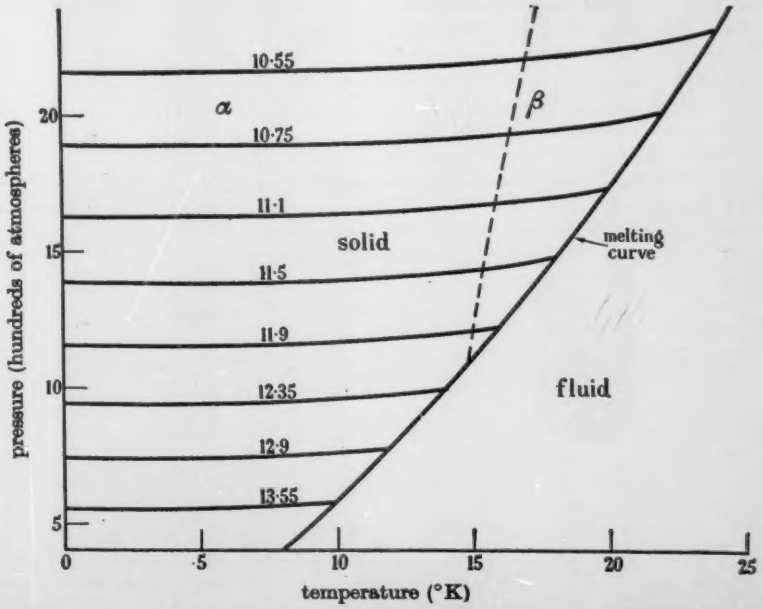


Fig. 3. Part of the melting curve of He^4 and the lines of constant volume in the solid. The figures give the corresponding molar volume in cubic centimeters. [After Dugdale and Simon (12)]

shown that this technique of applying pressure by means of solid helium does in fact produce a very close approximation to hydrostatic pressure (*9*).

Our measurements so far have been confined to the monovalent metals—in particular to copper and the alkali metals, except cesium (*9, 13*). Alkali-metal specimens used in the measurements of resistance at low temperatures have usually been enclosed in glass capillaries because the metals are chemically very reactive and mechanically very soft. For the measurement of pressure effects such specimens are not satisfactory, and we have used extruded bare wires mounted loosely on insulated formers; a photograph of such a specimen is shown in Fig. 4. The photograph shows the specimen mounted in position and ready to be enclosed by the high-pressure bomb, which is made of beryllium copper; the high-pressure seal is made by means of a steel lens ring.

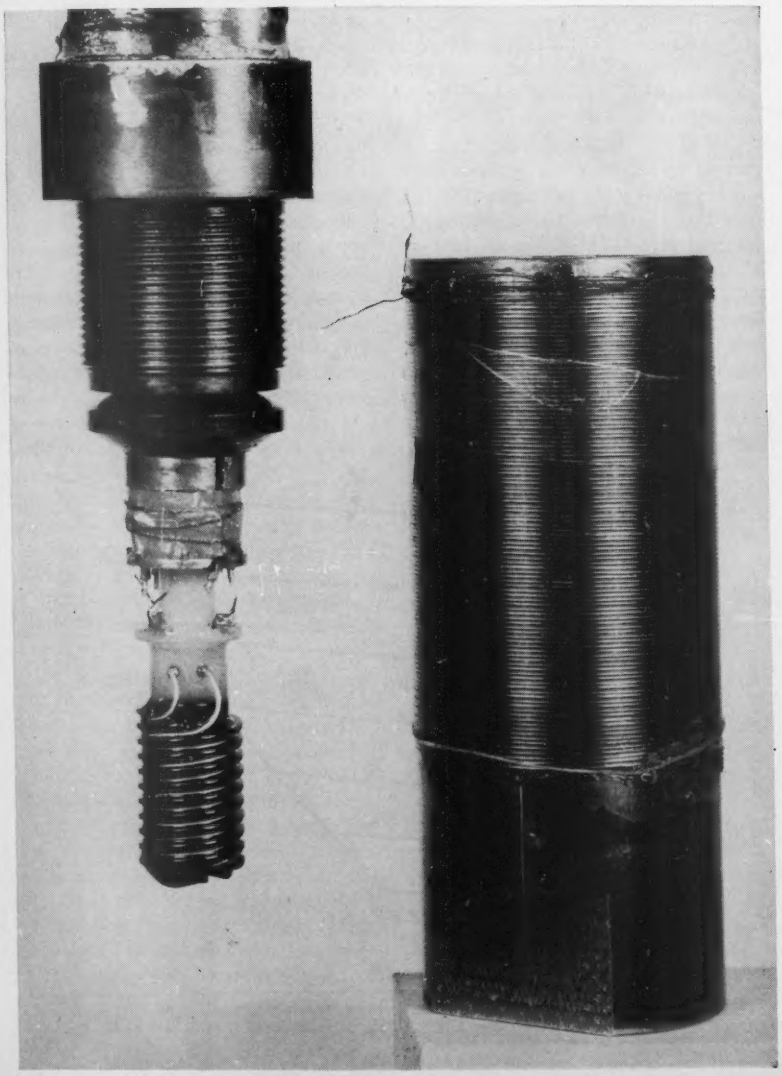


Fig. 4. A photograph of a typical alkali metal specimen wound on an insulated former. At right is the beryllium-copper bomb which encloses the specimen.

Expectations and Findings

As already mentioned, we expect a linear relation between the logarithmic volume coefficient of ideal resistivity and the logarithmic temperature coefficient of ideal resistivity. Figure 5 shows that such a linear relationship does in fact exist (*9, 13*) for those metals (lithium, sodium, potassium, and copper) for which the necessary data are available. In these graphs I am referring to the high-temperature modifications of sodium and lithium—that is to say, the body-centered cubic phases. At low temperatures both these metals partially transform to a close-packed phase; in lithium this transformation affects the pressure coefficient of resistivity so greatly that no reliable results have been obtained below about 75°K on this metal.

From the curves in Fig. 5 we can deduce for each metal the two quantities $d \ln \theta_R / d \ln V$ and $d \ln K / d \ln V$. These values are given in Table 1. For comparison, the Grüneisen parameter γ [or $- d \ln \theta_D / d \ln V$ (*14*)], which, as I showed earlier, can be evaluated from readily available thermodynamic data, is also included; it is evident that the change of θ_R with volume is quite similar to that of θ_D, as one might expect. Although accurate pressure measurements over a sufficiently wide temperature range have so far been made on only the four metals mentioned, the quantity $d \ln K / d \ln V$, which can be derived from high-temperature measurements only, by assuming that $- d \ln \theta_R / d \ln V$ equals γ (the Grüneisen parameter), has been derived for all the monovalent metals. The results are presented in Table 2 (columns 2, 3, and 4); the data for cesium are rather uncertain.

In order to understand why some of these values of $d \ln K / d \ln V$ are positive and why some are negative, it is necessary to digress and to explain something more of the behavior of the conduction electrons (*5*). Although it often gives a good approximation to imagine the conduction electrons moving through the ionic lattice as though they were free electrons (apart from the scattering processes which I have mentioned), it is in general necessary to take account of the fact that their motion is in fact modified by the periodic potential inside the static crystal. This can often be done by assigning an "effective" mass to the electron which differs from its true mass but takes account of interaction with the lattice potential. Another important feature of the electron motion arises from the fact that electrons obey the Pauli exclusion principle. At the absolute zero of temperature the electrons take up a configuration of minimum energy which, classically, would be one of zero kinetic energy—that is, with all the electrons at rest. Because of the

Table 1. Data on resistivity for lithium, sodium, potassium, and copper.

Metal	$-\frac{d \ln \theta_R}{d \ln V}$	Grüneisen parameter γ	$\frac{d \ln K}{d \ln V}$
Li	1.0	0.9	− 3
Na	1.3	1.3	+ 1.8
K	1.4	1.3	+ 2.9
Cu	2.3	2.0	− 1.8

exclusion principle, however, this is not possible, since each state of kinetic energy can be occupied by only two electrons (of opposite spin). Consequently the electrons "fill up" all the lowest kinetic-energy levels available to them until all the electrons are accommodated. Therefore, at the absolute zero of temperature all the lower kinetic-energy levels are filled up to a certain value E_o, and above this the levels are all empty. The value of E_o in a typical monovalent metal, if expressed as an equivalent temperature, is around 50,000°K—in other words, this is the temperature to which a classical electron gas would have to be heated to have a similar kinetic energy. It is evident from this that even at room temperature the additional kinetic energy of the electrons that is due to thermal motion is tiny as compared to their zero-point energy, so that for some purposes we can treat the electrons as being effectively at 0°K. The maximum energy E_o of the electrons at 0°K (or more generally, their chemical potential) is referred to as the Fermi energy of the electrons, E_F, and this quantity varies with volume; in the simplest approximation of quasi-free electrons, $E_o \propto V^{-2/3}$.

How are the electron velocities distributed over the various directions in space? In an ideal gas the distribution would be isotropic—that is, the average velocity would be the same in all directions. In discussing electrons in metals it is more convenient to work, not directly with the electron velocity or momentum, but (since the properties of electrons are governed by wave mechanics) with the electron's wave number k, which in the case of completely free electrons would be related to the momentum by the De Broglie relationship $hk = p$. The energy of such electrons (of mass m) is given by $E = h^2k^2/2m$, so if we plot the components of k, k_x, k_y, and k_z along cartesian axes (k-space), the surfaces of constant energy would therefore be spheres (corresponding to an isotropic distribution of velocities). The surface corresponding to the Fermi energy of the electrons is called the Fermi surface. If the electrons are not free but are influenced by the potential field of the lattice, then the Fermi surface will no longer be a sphere but will be more or less distorted, depending on the influence of the lattice potential; the symmetry of the Fermi surface taken as a whole is closely related to that of the crystal. The importance of the Fermi surface arises from the fact that only electrons close to the Fermi surface have unoccupied electronic levels in their neighborhood—in other words, these are the only electrons which can be thermally excited (at normal temperatures) or scattered by lattice waves or impurities.

The wavelike properties of electrons imply that, like x-rays, electrons in a crystal may suffer Bragg reflections. Thus, if an electron propagating in a certain direction in the crystal has just the right wavelength to satisfy the Bragg condition, it will be reflected by the appropriate lattice planes. Suppose that we choose some particular direction in the crystal and then find the minimum value of k which an electron propagating in that direction must have to satisfy the Bragg relation; suppose, further, that we do this for all possible directions. Then if we draw these k-vectors from the origin in k-space, it turns out that their ends lie on a polyhedron about the origin, this polyhedron having the symmetry of the lattice. This polyhedron is referred to as the first Brillouin zone of that lattice, and it is relevant to any kind of wave that can propagate through the lattice (in particular lattice waves and electrons). If for the electrons we draw surfaces of constant energy in k-space, all those surfaces lying within the Brillouin zone are continuous, whereas those surfaces which intersect the zone boundary will, in general, suffer a discontinuity; there is in fact a forbidden energy region at the zone boundaries such that electrons with energies lying within this range cannot propagate in the lattice.

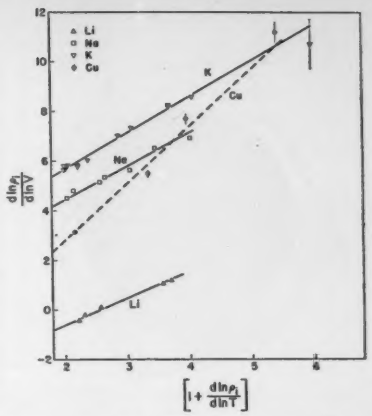


Fig. 5. The logarithmic volume coefficient of the ideal resistivity of lithium, sodium, potassium, and copper, shown as a function of the logarithmic temperature coefficient.

The volume of the zone in k-space is such that if the crystal has N atoms per unit volume (*15*), then the zone can accommodate N electrons of a given spin, uniformly distributed throughout the zone. Since electrons can exist in two independent spin states of the same wave vector, the zone can contain just $2N$ electron states.

This latter conclusion has the following important consequence. In a monovalent metal, which has just one conduction electron per atom, the Fermi surface which encloses all the electron states in k-space must therefore comprise a volume equal to half that of the Brillouin zone. This in turn means that if in cubic monovalent metals the Fermi surface is nearly spherical it can be entirely contained within the first zone without anywhere touching it. This

Table 2. Data on resistivity for the monovalent metals.

Metal	$\frac{d \ln \rho_i}{d \ln V}$ at 0°C	2γ	$\frac{d \ln K}{d \ln V}$	$\left(\frac{d \ln \rho}{d \ln E}\right)_V = x$	$\frac{d \ln K}{d \ln V} \Big/ x$	θ_o	θ_R*	θ_R/θ_o	$\frac{M\theta_o^2 V^{1/3} \rho_i}{T}$
Li	−0.49	1.8	−2.3	6.7	−0.3	369†	385†	1.04	7.2
Na	4.6	2.6	2.0	−2.7	−0.7	152‡	205‡	1.35	2.0
K	5.7	2.6	3.1	−3.8	−0.8	90	116	1.29	2.0
Rb	3.7	3.0	0.7	−2.3	−0.3	55	58	1.06	3.1
Cs	(4)	3.2		−0.2		40	45	1.13	4.4
Cu	3.0	4.0	−1.0	+1.6	−0.6	344	333	0.97	8.4
Ag	3.9	4.8	−0.9	+1.1	−0.8	225	223	0.99	6.3
Au	5.5	6.2	−0.7	+1.5	−0.5	165	175	1.06	13.5

* The value for cesium was taken from MacDonald (*1*). The other values of θ_R were taken from (*13*) and (*9*) for the alkali metals and from (*27*) for the noble metals. † Two-phase mixture. ‡ Estimated value for the body-centered cubic phase.

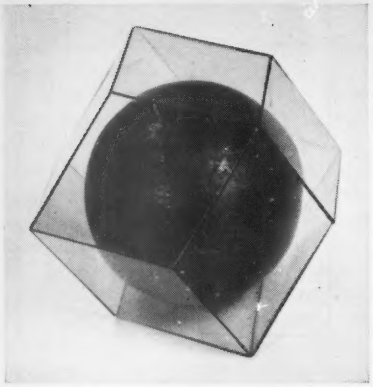


Fig. 6. A model of the first Brillouin zone of a body-centered cubic lattice. The sphere occupies half the volume of the zone.

situation is illustrated in Fig. 6, which shows a model of the first Brillouin zone of a body-centered cubic lattice containing a sphere whose volume is just half that of the zone. Figure 7 shows a two-dimensional square lattice, its two-dimensional Brillouin zone and the Fermi "circle" having an area of just half that of the zone. In Fig. 7 (*a*, *b*, *c*, and *d*) I have shown, purely schematically, the progressive distortion of the Fermi surface; in *d* this surface is in marked contact with the Brillouin zone. In general, distortion of the Fermi surface causes those regions which are nearest the zone boundaries to become even closer.

A great deal is now known about the Fermi surfaces of the noble metals from a variety of techniques which give direct information about the shape and other features of the Fermi surface (*16*). These methods agree in showing that the Fermi surfaces in copper, silver, and gold all touch the zone boundary. About the alkali metals we have as yet no direct evidence, but indirect evidence suggests that the Fermi surfaces of sodium and potassium are nearly spherical, that the Fermi surface of rubidium is somewhat distorted, and that the Fermi surfaces of lithium and cesium are much more distorted, perhaps touching the Brillouin zone boundary (*17*, *18*). The effects of such distortion on electrical resistivity are discussed later.

When an electric field is applied to a metal the conduction electrons are accelerated and the whole Fermi surface begins to move in the direction of the field (see Fig. 8). The electrons, however, are prevented from continuous acceleration in the field by collisions with phonons (we are considering only the ideal resistivity), and the Fermi-surface movement is almost vanishingly small. The effect of the distortion of the Fermi surface on the scattering of electrons by phonons is a difficult theoretical problem, and detailed studies have only recently been made (*19*). One of the most important effects arises from a type of scattering process called an "Umklapp" process, which gives rise to large angle scattering of the electrons.

First consider a typical *normal* scattering process in which an electron of wave vector k is scattered by a phonon of wave vector q into a new state of wave vector k'; k, k', and q are related by the vector condition that $k - k' = q$. Moreover, the phonon energy at all normal and low temperatures is very small compared with the Fermi energy of the electrons. Since only those electrons near the Fermi level have neighboring unoccupied states into which they may be scattered, the scattered electron must both start and end effectively at the Fermi surface. Figure 9 shows the geometry of a normal scattering process. As mentioned earlier, the Brillouin zone governs the behavior of all kinds of waves that can propagate through the metal, including lattice waves; the biggest wave vector that a phonon can have is one which reaches from the center of the zone to the zone boundary. This therefore limits the angle through which an electron may be scattered in a normal process, even at the highest temperatures. At low temperatures, where only low-energy phonons (having therefore small wave vectors) are excited, the angle of scattering is even further limited in such processes.

An Umklapp process may be interpreted as one in which the electron is scattered by a phonon and also undergoes a Bragg reflection. In vector terms, the well-known Bragg condition is represented by the equation $k' - k = R$, where R is a reciprocal lattice vector. In Fig. 7 the vectors R' and R'' are two reciprocal lattice vectors for the simple square lattice. Thus, in an Umklapp process the vector condition

$$k' - k = q \tag{7}$$

is replaced by

$$k' - k = q + R \tag{8}$$

where R is a reciprocal lattice vector. Such a process is illustrated in Fig. 10. Its importance lies in the fact that, because the large vector R enters into the process, it makes possible scattering at wider angles than can occur in a normal process. This can also be seen by a geometrical construction. Equation 8 may be rewritten as

$$k + R = k' - q$$

and we begin by representing graphically all the possible vectors $k + R$. Since the k vectors of all electrons which can be scattered must lie on the Fermi surface, the vectors $k + R'$, for example, must lie on the same surface displaced by the vector R'; the same is

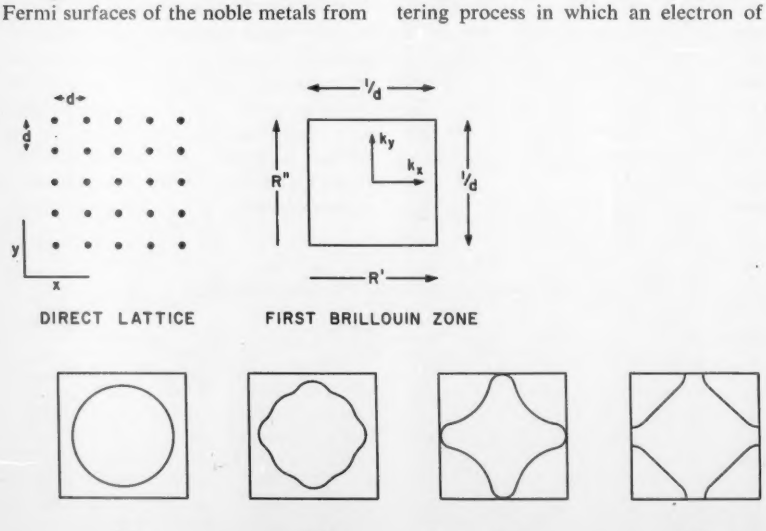
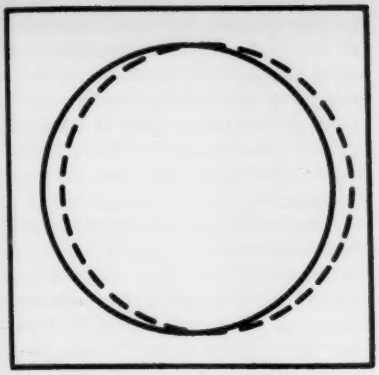
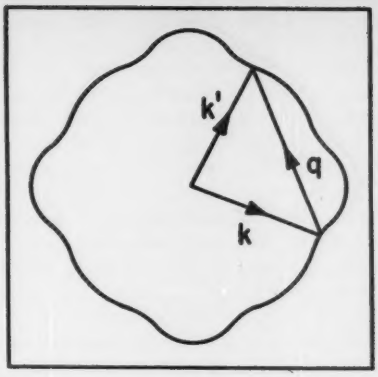


Fig. 7. A two-dimensional square lattice and the corresponding first Brillouin zone. (*a*) The Fermi "circle" corresponding to one electron per atom; (*b*), (*c*), and (*d*), progressive distortions of the Fermi surface (schematic).





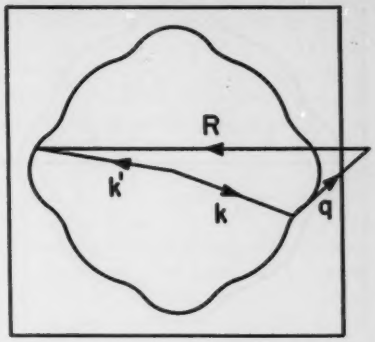


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Fig. 8 (left). Displacement of the Fermi surface under the influence of an electrical field. Fig. 9 (middle). A "normal" scattering process. Fig. 10 (right). An Umklapp process.

true for the other reciprocal lattice vectors. Thus, the possible $k + R$ vectors lie on a set of surfaces consisting of the original Fermi surface suitably displaced, as in Fig. 11. In order to satisfy the requirement of conservation of energy, all the vectors k' of the electrons after scattering must lie on the original Fermi surface; so, to satisfy Eq. 8, we must look for vectors $-q$ which go from one of the repeated Fermi surfaces back to the original Fermi surface. Such phonon vectors, illustrated in Fig. 11, give rise to Umklapp processes.

If the Fermi surface does not touch the zone boundary, then q must exceed a certain minimum value or else Umklapp processes are impossible. This minimum value is equal to the distance of closest approach of two adjacent Fermi surfaces—for example, the vector CD in Fig. 11. An Umklapp process with this minimum vector scatters the electron through the maximum angle of 180° (Fig. 12). q vectors which are larger than the minimum usually produce rather smaller scattering angles; nevertheless all Umklapp processes in a monovalent metal cause comparatively large angle scattering.

The existence of a minimum value of q for Umklapp processes means that at low temperatures the number of such processes must begin to fall off because the number of phonons with a large enough wave vector begins to fall off. Thus, the shape of the Fermi surface can influence the temperature dependence of electrical resistivity at low temperatures. It also affects the magnitude of the resistivity, since at all temperatures the more closely the Fermi surface approaches the zone boundary the greater is the number of phonons that can take part in Umklapp processes. Since, as has been emphasized, these are wide-angle scattering processes, this implies that the nearer the Fermi surface is to the zone boundary the higher is the electrical resistivity, other things being equal. (By "other things" I mean in particular the number of phonons available for scattering the electrons; this point is discussed in more detail in the next paragraph.) Distortion of the Fermi surface changes not only the number of possible Umklapp processes but also, for example, the velocity of the electrons at the Fermi level, and this too can alter the resistivity. In general, however, it seems that, if the resistivities of the monovalent metals are compared under conditions such as

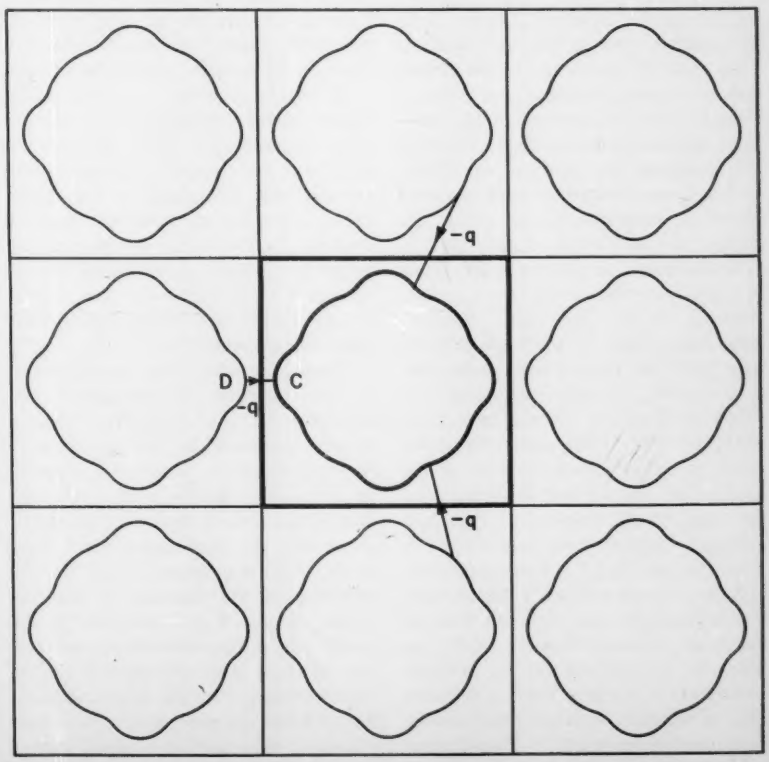


Fig. 11. Repeated zone scheme to illustrate the possible wave vectors which can give rise to Umklapp processes.

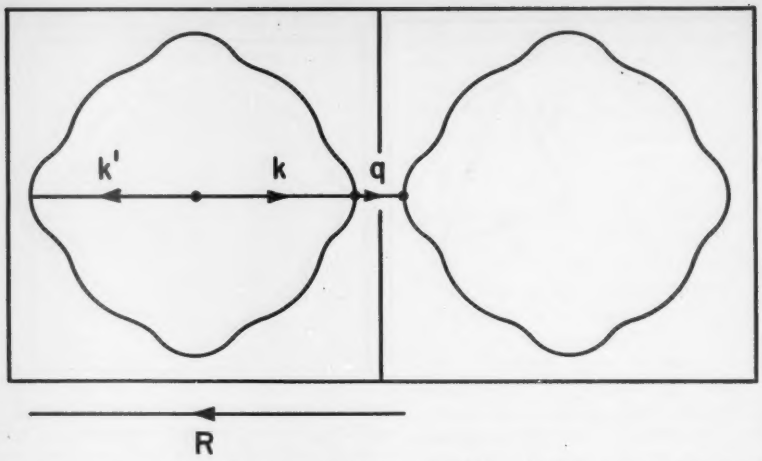


Fig. 12. Electron scattering through 180° by a phonon having the minimum wave number which can cause an Umklapp process.

to eliminate the effects of their different lattice properties, the more distorted the Fermi surface the higher the resistivity. With these ideas in mind let us now look at the magnitude of the resistivities of the monovalent metals.

In comparing the resistivity of different metals it is important to compare not the resistance ρ of a cube of side 1 centimeter but rather that of a cube containing, for example, 1 gram atom of material—that is, the atomic resistivity $\rho/V^{1/3}$ where V is the gram-atomic volume. Moreover, in order to bring out the dependence of the resistivity on the properties of the electrons (for example, the shape of the Fermi surface), the resistivities must be compared at temperatures at which the lattices are in similar states—that is, at temperatures at which the amplitude of the lattice vibrations is some certain fraction of the interatomic distance. This means that, in the high-temperature "classical" region, one should compare not the atomic resistivities but rather the "reduced" atomic resistivities $\rho(M\theta^2V^{1/3}/T)$. (The derivation of this result is rather similar to that of the Lindemann melting formula; here M is the mass of the ions and θ, the characteristic lattice temperature.) The actual temperature T is immaterial since at high temperatures ρ/T tends to reach a constant value and it is this limiting value, at constant density, which we take. A comparison of the reduced resistivities is made in Table 2 (column 10), in which θ_o is taken from specific heat measurements (*20*). These Debye θ_o values, which can be taken as a measure of the temperature dependence of the phonons, are now quite well established, although in sodium and lithium the low-temperature crystallographic transformations introduce some uncertainty. I should also point out that, since the noble metals have a face-centered cubic structure while the alkali metals have a body-centered cubic structure (except for sodium and lithium at low temperatures), the comparison between the two sets of metals cannot be taken too literally, although the general features should be correct.

It may be seen that of all the monovalent metals, potassium and sodium are outstandingly good conductors, rubidium and cesium are successively poorer, and lithium and the noble metals are worse still. Among the noble metals, silver has the lowest reduced resistivity. This classification corresponds broadly with what is at present known about the Fermi surfaces of the monovalent metals.

Having considered the magnitudes let us now consider the temperature dependence of the resistivity. This is largely governed by the temperature dependence of the number of phonons in the lattice—that is, by the Debye θ_o. But as we saw in discussing Umklapp processes, the low-temperature resistivity does not depend only on the behavior of the phonons; it also depends on the Fermi surface. If the metal has a distorted Fermi surface, the electrical resistivity tends to remain higher (because of the increased number of Umklapp processes) at low temperatures than that of a metal with a spherical Fermi surface at the same reduced temperature (that is, with the same number of phonons excited). Roughly speaking, θ_R (which is a measure of the temperature dependence of ρ_i) is proportional to the lowest temperature at which ρ_i behaves classically —that is, the temperature at which ρ_i departs from linearity with T. This temperature should therefore be lower for metals in which Umklapp processes can persist to lower temperatures. Thus, we should expect θ_R/θ_o to vary with the degree of distortion of the Fermi surface; for a metal with a distorted Fermi surface the ratio should be lower than for a metal with an undistorted Fermi surface. The values of this ratio are given in Table 2 (column 9), and they show roughly the sort of variation we should expect: sodium and potassium have exceptionally large values for the ratio, the other metals have lower values. Interestingly enough, these lower values are all close to unity; why the values of θ_o and θ_R should be about equal for these metals is not, I think, altogether understood.

These comparisons suggest that the pressure coefficients might likewise be understood, at least qualitatively, in terms of distortion of the Fermi surface. Table 2 (column 4) shows that the values of $d \ln K/d \ln V$, which measure the change of interaction constant with volume, do fit into the pattern. For example, all the noble metals have negative values and so does lithium. These are the monovalent metals with the most distorted Fermi surfaces. Sodium and potassium, the two metals with nearly spherical Fermi surfaces, have values of $d \ln K/d \ln V$ which are decidedly positive; rubidium has an intermediate value. For cesium the data needed here are not reliable, but as we shall see below, cesium too fits into the general picture.

Although there is a clear correlation between the pressure coefficients of resistivity and distortion of the Fermi surface, we still have to understand why in a metal with a spherical Fermi surface $d \ln K/d \ln V$ is positive whereas in a metal whose Fermi surface touches the zone boundary it is negative. This is a theoretical problem which has not yet been fully solved. Nevertheless, let us consider first the example of a spherical Fermi surface which, for simplicity, we shall assume does not distort under pressure (*21*). A positive value for $d \ln K/d \ln V$ means that a decrease in volume causes the electrons to interact less with the lattice waves. Decreasing the volume increases the Fermi

energy of the electrons, and we may interpret this result as meaning that as the electron energy is increased the electrons are less scattered by the lattice waves. This conforms with the classical idea that a body with greater kinetic energy is scattered less by a given obstacle than one with lower energy.

We have here assumed that on compression of the lattice the Fermi-surface distortion remains unchanged. While this may be true of sodium for small volume changes, theoretical calculations show that this is not generally true (*18*). In general, in all the monovalent metals, increasing the pressure on the metal increases the distortion of the Fermi surface; if the surface is already touching the zone boundary, pressure will increase the area of contact. Such an increase in the distortion of the Fermi surface under pressure, with the consequent enhancement of Umklapp processes, tends to increase the resistivity. This was originally proposed as an explanation of the anomalous positive pressure coefficient of resistance in lithium (*17*), and it seems probable that the same basic mechanism occurs in all the monovalent metals.

There are thus two opposing tendencies when a metal is compressed—on the one hand an increasing distortion of the Fermi surface, which increases the interaction constant K, and on the other hand an increase in the Fermi energy, which, as suggested above, tends to decrease K. The trend of the values for $d \ln K / d \ln V$ leads us to suppose that the more distorted the Fermi surface is, the more prominent the first effect becomes. This is perhaps plausible, but without a careful theoretical analysis it is not possible to say more. Unfortunately such an analysis has not yet been made. Nonetheless, quite empirically, it does seem that in the monovalent metals, negative values of $d \ln K / d \ln V$ are associated with a Fermi surface already in contact with the zone boundary, and the large positive values, with a nearly spherical Fermi surface. We might therefore guess that if this parameter is about zero this indicates that the Fermi surface is just about to touch the zone boundary.

Bridgman (*22*) has measured the pressure dependence of the electrical resistance of the alkali metals at room temperature up to very high pressures. It is interesting to consider these curves in terms of the distortion of the Fermi surface which we have just been discussing. Bridgman's results are shown in Fig. 13, in which relative resistance is shown as a function of the relative volume. As I have already emphasized, an important part of the change in ideal resistivity with volume arises from the change produced in θ. It is possible, from a knowledge of the compressibility of the lattice as a function of volume, to estimate how θ changes with volume. Using this information and that in Fig. 13, I have estimated how the interaction constant K changes with volume over the full range of pressures; these results are shown in Fig. 14. Lithium is remarkable in that, for it, K always increases under compression; this has already been discussed. The curve for cesium shows a pronounced minimum when its volume has been reduced by about 5 percent. We can now interpret this to mean that at this volume (approximately), contact of the Fermi surface with the Brillouin zone boundary occurs. The behavior of rubidium is rather similar, although for it the

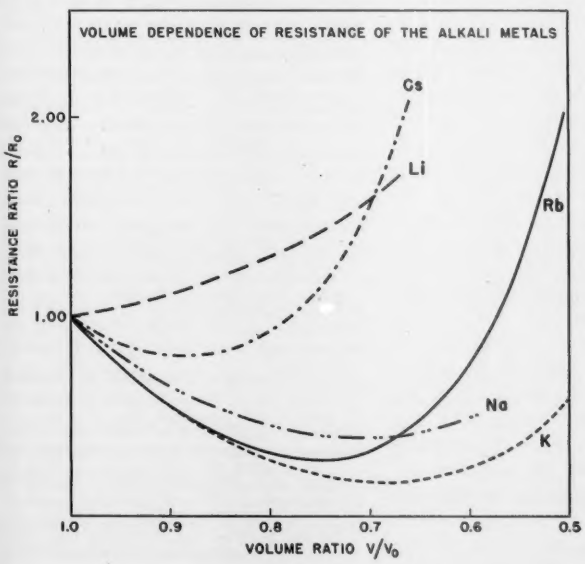
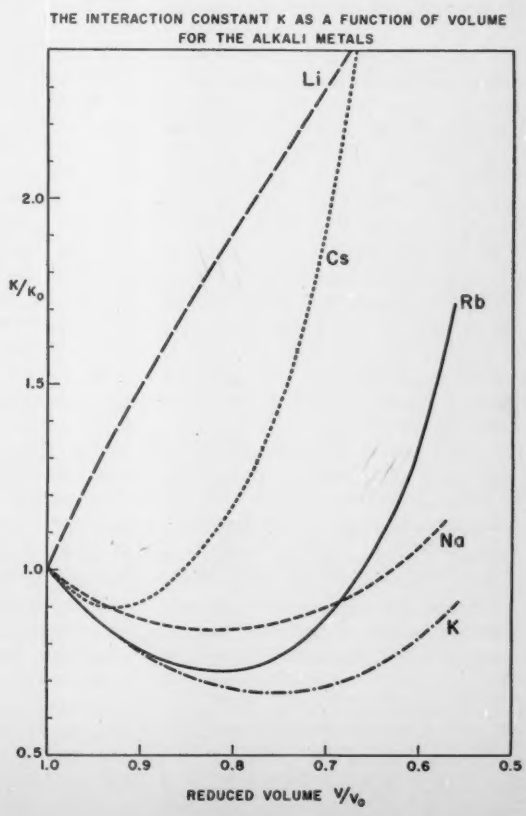


Fig. 13 (above). The change in electrical resistance with volume of the alkali metals at 0°C. [From Bridgman (*22*)] Fig. 14 (right). The change in interaction constant K with volume for the alkali metals. [Derived from Fig. 13]



minimum is reached at a rather higher pressure. Sodium and potassium behave rather differently from the others: for these two metals K increases rather slowly after the minimum has been reached. Nevertheless it seems that in all these metals we are seeing the effect on K of progressive distortion of the Fermi surface.

Pressure Coefficients and Thermoelectric Power

At high temperatures (temperatures which are large as compared to the characteristic temperature of the lattice) the absolute thermoelectric power of a metal S is related to its resistivity by the following relationship (*23*):

$$S = -\frac{\pi^2 k^2 T}{3eE_F}\left(\frac{d \ln \rho(E)}{d \ln E}\right)_{E=E_F} \quad (9)$$

(k is Boltzmann's constant and e is the electronic charge). This relationship (*24*) expresses the fact that the thermoelectric power of a metal depends on how the resistivity of the metal varies with its Fermi energy, and from the measured values of the thermoelectric power of a metal at high temperature it is thus possible to obtain a measure of this variation through the quantity

$$x = \left(\frac{d \ln \rho(E)}{d \ln E}\right)_{E=E_F}$$

One way of altering the Fermi energy of a metal is to compress it. Thus there should be some relationship between the volume coefficient of resistivity and the value of x for that metal. It is not to be expected that x will be related to the *total* change of resistance due to the volume change because this involves the change in the amplitude of the lattice vibrations, which has no counterpart in x. If, however, we eliminate the part due to changes in the lattice vibrations and consider $d \ln K/d \ln V$, we might expect that this would be related to x. In Table 2 a comparison of these quantities is made for the monovalent metals, and the ratios are listed (column 6). If the change in K with volume were due entirely to the change in the Fermi energy E_F with volume and if the Fermi surface did not distort under pressure, this ratio would be simply $d \ln E_F/d \ln V$. For a spherical Fermi surface this has the value $-2/3$, since E_F is proportional to $V^{-2/3}$. It may be seen that for all the metals the value lies between -0.3 and -0.8; in particular for sodium and potassium, the two metals whose Fermi surfaces are most nearly spherical, the value of the ratio is quite close to $-2/3$.

If the interpretation given above of the minimum in the resistance-versus-pressure curve of cesium is correct, and if the thermoelectric power is intimately related to the quantity $d \ln K/d \ln V$, the thermoelectric power of cesium should be very sensitive to pressure and should in fact change sign at quite modest pressures (pressures similar to that required to reduce the resistance to its minimum value). Recent measurements on the thermoelectric power of cesium at 0°C (*25*) show that this change of sign does indeed occur and that the thermoelectric power of cesium is extremely sensitive to pressure; it changes by nearly 1/2 percent per atmosphere.

To sum up, we may say that the pressure coefficient of the ideal resistivity of a metal changes appreciably only at low temperatures ($T < \theta/3$); moreover, experiments show that this change is related to the change in the temperature coefficient of resistivity in the way that theory predicts. There appears to be a close connection between the electronic contribution to the pressure coefficient of resistance on the one hand and the thermoelectric power of the metal on the other. When one comes to consider the magnitude of the pressure coefficient it is clear that in some metals, notably lithium, cesium, and the noble metals, this can only be understood in terms of the distortion of the Fermi surface of the metal. This distortion is also reflected in the temperature dependence and the magnitude of the resistivity. All this emphasizes how desirable it would be to obtain *direct* information about the shape of the Fermi surfaces in alkali metals (*26*).

References and Notes

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20. θ_0 is the limiting value of the Debye θ at the absolute zero of temperature.
21. Even under compression the Fermi surface must continue to occupy the same proportion of the Brillouin zone (here, one-half). If, therefore, the *shape* of the surface does not change under compression, the geometry in k-space of the scattering processes is unchanged.
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26. It is a pleasure to acknowledge the collaboration of Dr. D. Gugan in much of the experimental work described here. I am very grateful to Dr. D. K. C. MacDonald for his encouragement and interest at all times and wish to thank him and Dr. A. V. Gold for many valuable discussions and for reading the manuscript.

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Shark Attacks

Worldwide records through 1960 show when and where predaceous sharks are likely to attack man.

Leonard P. Schultz, Perry W. Gilbert, Stewart Springer

In August 1960 an article by us appeared in *Science*, entitled "Shark attacks during 1959: The conditions under which sharks attack man suggest what measures may be taken to reduce risk" (*1*). We have continued our studies on this subject, and the "Shark Attack File" for the world, sponsored by the Biology Branch of the Office of Naval Research, the Smithsonian Institution, and Cornell University, has been maintained and expanded.

When members of the Shark Research Panel of the American Institute of Biological Sciences receive word of a shark attack anywhere in the world, an attempt is made to obtain documentation from reliable witnesses, doctors, hospitals, police departments, scientists, and others. A two-page form requesting information concerning the details of the attack is sent to those who are willing to collaborate in supplying documentation. The "Shark Attack File" is under the direction of Leonard P. Schultz in the Division of Fishes, Smithsonian Institution, Washington, D.C. A duplicate current working file is maintained by the chairman of the Shark Research Panel, Dr. Perry W. Gilbert at Cornell University, Ithaca, New York.

In our article (*1*) we summarized recommendations and other pertinent advice to those who enter the domain of dangerous sharks. We have little to add to our advice to bathers, swimmers, SCUBA divers, skin divers, and survivors of air and sea disasters.

Kinds of Attack

We have continued to record shark attacks in the file at the Smithsonian Institution, under "unprovoked" attacks (*2*) and attacks in four other categories. There were 30 unprovoked attacks during 1960, many involving severe injuries. Some of the victims were skin diving or spearfishing at the time of attack; others were swimming and bathing, some inshore, one 150 feet offshore, one in the open sea. There were four fatalities.

Attacks were recorded in other categories as follows.

1) "Provoked" shark attacks (*3*). There were 11 instances in 1960 in which a shark was "provoked" and subsequently attacked a man. Three anglers were severely bitten while hauling sharks into a boat; six commercial fishermen, in their attempt to untangle sharks from nets or traps, were attacked. One skin diver was attacked by a shark he had speared, and a lifeguard was knocked off a surf ski. There were no fatalities in this category.

2) Air and sea disasters. There were two instances during 1960 in which "unprovoked" sharks mutilated victims of such disasters. Often there is no way of knowing whether the victims died before the sharks attacked or died as a result of the attacks. Seven persons were involved. There were no survivors.

3) Boat attacks. There were 12 instances during 1960 in which "unprovoked or provoked" sharks made deliberate physical contact with a boat, life raft, water ski, or accessory equipment. There was no fatality among individuals in the boats.

4) Doubtful shark attacks. This category includes five instances in 1960 in which unprovoked sharks approached swimmers but failed to make physical contact with them; it also includes reported shark attacks which subsequent investigation tends to discredit or place in some doubt. Victims from drowning, other than those involved in air and sea disasters, whose bodies were mutilated by sharks are placed in this category.

Analysis

Since reporting on shark attacks for 1959 we have started to tabulate and analyze some of the factors related to shark attacks, as recorded in our files. An analysis of the 790 attacks recorded from the year 1580 to 31 December 1960 indicates that 599 were unprovoked, 42 were provoked, 30 resulted from air and sea disasters, 53 were doubtful, and 76 were boat attacks. We believe a summary based on the data in our files will be of general interest.

In the following analysis we were reasonably careful to exclude unreliable data, because we are well aware that documentation grades from excellent to poor. The latter type of information usually includes only locality, date, and sometimes name of victim, obtained through newspaper accounts. Therefore, although we studied 599 instances of "unprovoked" attack, we may have reliable information about certain facts and circumstances, for example, on only 68 individuals. In the paragraphs below we give the number of instances for which the information appears reliable.

Time of Day

The peak period for bathing is during the daylight hours, from 8:00 A.M. to 7:00 P.M., and this corresponds with the period of the day when most shark attacks occurred. Our records show that most attacks occur between 11 o'clock in the forenoon and 6 o'clock in the afternoon—findings based on 159 instances in which the time of attack was carefully recorded. When our data are expressed in percentages we find that 3.1 percent of the attacks occurred between midnight and 6:00 A.M.; 22 percent between 6:00 A.M. and noon; 66.7 percent between noon and 6:00 P.M.; and 8.2 percent between 6:00 P.M. and midnight.

We pointed out above that most of the shark attacks occurred between 11:00 A.M. and 6:00 P.M., presumably the peak period for swimming. Actually, our figures indicate that 94.3 percent of all attacks occurred during

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daylight hours (from 5:00 A.M. to 7:00 P.M. in tropical regions), whereas only 5.7 percent occurred during darkness.

The question arises, How does the number of swimmers and bathers after dark compare with the number during daylight hours? Although we have no data on that point, we believe that the number of people in the water after dark is significantly less than 5 percent of the number in the water during daylight hours. If that is true, then it is more dangerous to swim at night than in the daytime. Since we need counts of the number of bathers in the water for each hour of the day and night, lifeguards are urged to cooperate in supplying this information.

Time of Year

The time of the year when most attacks occur correlates closely with the swimming season. Around Australia and Africa, 75.4 percent of all attacks have occurred during the summer (from mid-November to mid-April), whereas in North America, 73 percent of the attacks have occurred from mid-May to late September. Northern Australia, the equatorial regions of the Indian and Pacific Oceans, and southern North America are tropical all the year, and in such warm waters, where presumably bathing is not seasonal, shark attacks occur in nearly equal numbers for each month.

Area of Attack

The greater frequency of shark attacks in water warmer than about 65°F was first noted by Stewart Springer in 1943. Two factors at least contribute to this greater frequency. First, the more dangerous kinds of sharks, such as the great white, tiger, and gray sharks (*Carcharhinus*), typically are in greatest abundance in warm waters, and when the seas and river waters become warm during the summer in temperate zones, the "tropical" sharks enter these waters. Second, relatively few swimmers enter water colder than about 65°F. Thus, the warming up of temperate waters is accompanied by an increase in the number of dangerous sharks and an increase in the number of bathers.

However, divers with swim suits do enter colder waters, and three attacks have occurred in water at 55°F along the California coast. We believe that the area of shark attacks will expand as more and more divers enter the domain of predaceous sharks in the temperate and subtemperate latitudes.

The largest number of shark attacks occur in the areas where bathers are most thickly congregated, usually close to shore. Relatively few bathers venture beyond a few hundred feet from the beach. We have 217 reliable records of the distance from shore at which sharks attacked, and we find that 38.2 percent were within 100 feet of the shore; 16.6 percent were from 101 to 200 feet from shore; 7.4 percent from 201 to 300 feet; 8.3 percent, from 301 feet to a quarter of a mile; 10.6 percent, from a quarter of a mile to 2 miles; and 18.9 percent, in the open sea. In summary, 62.2 percent of the attacks occurred within 300 feet of the shore. This is the area where swimmers are concentrated.

The depth at which sharks most commonly attack coincides with the depth at which there is the greatest concentration of bathers. Of 302 individuals attacked, 212, or 70.2 percent, were in the upper 5 feet of the surface waters, and 75, or 24.9 percent, were in water more than knee-deep and no more than shoulder-deep at the time of attack. Only 15, or 4.9 percent, were between 5 and 80 feet below the surface.

A review of the activities of 360 individuals just before being attacked by sharks indicates that 75, or 20.8 percent, were wading or standing in water knee-deep to chin-deep; 37, or 10.3 percent, were swimming or standing close to where fish were swimming or being caught; 19, or 5.3 percent, were spearfishing or diving and carrying fish; 23, or 6.4 percent, were resting, floating, or clinging to a float at the surface; and 206, or 57.2 percent, were swimming at the surface. Our data reveal that it is dangerous to dive off piers, boats, and ships at anchor in shark-infested bays and lagoons, for we have several records of divers who were attacked under such circumstances the moment they entered the water.

Our files include information on the location of companions and other swimmers in relation to the position of the victim of shark attack. Of 165 individuals, 63, or 38.2 percent, were alone in the water when attacked; an additional 18, or 15.8 percent, were 10 or more feet away from companions; 35 (21.2 percent) were within a few feet of one other person when attacked; and 41, or 24.8 percent, had companions 4 to 10 feet away.

How dangerous is it to try to rescue someone being attacked by a shark? Our records indicate that of 68 individuals who have gone to the aid of a victim of shark attack, 12, or 17.7 percent, have been attacked. Hence, anyone going to the aid of a person being attacked is definitely placing himself in a dangerous situation.

Weather and Physical Factors

Weather and other physical factors do not appear to be especially significant in triggering shark attacks. For example, the number of attacks when the sky is clear and the number when the sky is cloudy are about equal. We have no evidence that a particular color of clothes or shade of skin is an important factor in stimulating sharks to attack. Bright shiny objects, or contrasting light and dark objects, do attract the attention of sharks. However, our data are too scanty and unreliable at present to suggest significant conclusions about physical factors.

The condition of the water—whether clear or murky—may be of importance because in murky water, as at night, the swimmer is unable to see the approaching shark and avoid it. Many swimmers have pointed out that they were able to ward off an attacking shark in clear oceanic waters.

At the time this article was prepared, our records revealed the following figures on recovery after unprovoked attacks: 390 individuals recovered, 408 died. High mortality occurred in regions where medical care was not immediately available.

In closing we want to say again that it is well established that fresh blood, even diluted and in small quantities, attracts and excites sharks (*4*).

References and Notes

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3. "Provoked" attacks include all cases in which a shark was caught, trapped, speared, injured, or in some way provoked before attacking the victim or the gear he was wearing. Although the use of the terms *unprovoked* and *provoked* may raise questions regarding separation of attacks into two such categories, we believe it is desirable to make this distinction because it emphasizes what sharks may do when annoyed or injured.

4. Marilyn Malin assisted with the documentation of the "Shark Attack File," as well as in other ways. We gratefully acknowledge her able services.

Science and the News

The Drug Hearings: To No One's Surprise, Kefauver and the AMA Do Not Agree on What Should Be Done

Senator Kefauver resumed his subcommittee's hearings on the drug industry last week, and two days of testimony from officials of the American Medical Association revealed, to nobody's surprise, that the AMA is unenthusiastic about the bill Kefauver has introduced to reform the drug business.

The first phase of the hearings was described here in two reports a year ago (*Science*, 29 April and 17 June 1960). These took the form, pretty much, of an exposé of what Senator Kefauver and his staff felt to be abuses by the major companies of their economic power which led to excessively high prices for drugs. Kefauver issued a lengthy report, signed by the Democrats on the committee, summing up his indictment of the industry. The Republican members, Dirksen of Illinois and Hruska of Nebraska, added a briskly worded minority report summing up their indictment of Kefauver's investigation.

Kefauver has produced a broad set of charges against the industry that ranges from misleading advertising to suggestions of illegal price fixing; but the heart of his complaint is that the major firms, through the use of exceptionally heavy promotion expenses, have been able to persuade the medical profession to write their prescriptions in terms that assure the companies exceptionally high profits (about double the average for other industries) without offering the public any important health benefits. The public ends up paying both for the high profits and for the heavy promotion that makes the high profits possible.

For the minority, Dirksen and Hruska answered with an equally wide-ranging set of charges against the way Kefauver ran the investigation and the conclusions he drew from it. But the essential point, in their view, is that the drug industry is providing the public with the best drugs available anywhere in the world; that the cost of these drugs is perfectly reasonable, and indeed cheap, compared with the good they do; and that Kefauver's proposals amount to an unwarranted attack on the free-enterprise system.

Current Hearings

The current phase of the hearings is being held to consider specific legislation. Technically, at least, the investigation is over, although Kefauver has taken the unusual step for a legislative (as opposed to an investigative) hearing of ordering several advertising agencies and medical publications to appear at the hearings along with their records. (Normally the witnesses at a legislative hearing appear voluntarily to give their views on the bill under consideration.) The hearings, under these circumstances, will probably begin producing headlines again as Kefauver seeks to document the extent of the industry's promotional effort, and the possible effect that the advertisers have on medical publications, from which the doctors are expected to receive unbiased information about new drugs.

The bill Kefauver has introduced is a so-called "omnibus bill" in which a variety of legislation bearing on the same general subject is combined into a single bill. The Kefauver bill includes amendments to the patent laws, the antitrust laws, the Food and Drug Act, and several other pieces of basic legislation, all of which are intended, directly or indirectly, to reduce the market power of the major drug firms.

Kefauver, for example, would amend the patent laws in two important ways. One would require a drug manufacturer to license his competitors to produce any drug on which he holds a patent. The licensee, of course, would have to pay for permission to market the patented drug, but the license fee would be limited to some small percentage (in the draft bill, 8 percent) of sales. The intent here is to meet the situation now common in which a patented drug is available only from the patent holder and perhaps two or three other firms, all of which charge essentially the same price. In Kefauver's view this price is usually unwarrantedly high. In Kefauver's view, if the drug were widely licensed there would be far more likelihood that competition would force the price down to a reasonable level.

The second change in the patent laws is intended to meet the problem of what is called "molecule manipulation." Kefauver has produced evidence that a sizable proportion of the new drugs patented and put on the market are not in any significant way new. They involve merely minor changes in the molecular structure of an already available, and perhaps unpatented, drug; their only advantage is that they can be patented, promoted as a new drug, and thus be relieved of direct competition with similar drugs identical in their medical effects. The Kefauver bill would require that a drug be significantly different in its effects as well as in the details of its molecular structure in order to be patentable.

AMA Testimony

The AMA testimony last week offered no comment on several of the provisions in the draft bill on the grounds that they involved economic rather than medical considerations. The patent licensing requirement was an example. On the provisions more directly connected with the AMA's professional field, the AMA spokesmen found nothing they could approve. Kefauver wants the government to have the power to decide what the generic names of drugs should be, on the grounds that the drug companies prefer to have the generic name sufficiently awkward to make it easier for the doctor to remember the trade name and use it when he writes a prescription. The AMA sees no need for the government to get involved in this, for the AMA has a committee to make recommendations in this field. Kefauver argued that there is need for someone outside the drug industry to have more power than merely to make recommendations.

On a more important point, Kefauver wants the Food and Drug Administration to be able to require proof of efficacy as well as proof of safety before it authorizes the marketing of a new drug. To some extent the FDA already has this power, for most drugs carry the possibility of harmful side effects, and a judgment on safety necessarily involves some balancing of the

benefits of the drugs against the possibility of side effects. But FDA has argued in the past that it should have direct power over efficacy on the grounds that any ineffective drug, even without side effects, is harmful since its use deprives a patient of treatment by another, perhaps more effective, drug.

The AMA argued that the FDA's powers should not be broadened, on the grounds that it is only through wide use that a clear idea emerges of the value of a new drug, and that there should be more cause for concern over keeping a possibly useful drug off the market than of allowing a useless drug to be sold. The AMA argued that it is just beginning an extensive program to keep the profession better informed on the latest evidence on the effects of new drugs, alleviating the need for government action in this field, and that except in very clear-cut cases, no one, not even the government, should have the power to interfere, as by keeping a drug off the market, with the judgment of the doctor as to what is the best treatment for a particular patient.

Kefauver professed to be unimpressed by the AMA testimony. The AMA, in assessing the efficacy of drugs, could not, like a government agency, require the drug companies to cooperate by supplying all the pertinent information from their files, including what might be unfavorable. On a broader question, Kefauver doubted whether it was reasonable to assume that the AMA could do a proper job of policing the advertising and promotional policies of the drug industry when it was dependent on the industry, through some $4 million annually of advertising in AMA journals, for over half its annual budget.

The debate comes down to a judgment on the degree of sanctity with which the partisans view the free enterprise system. To Kefauver, and to liberals generally, the situation in the drug industry is peculiarly offensive, both because the extra cost of drugs under the present system, although not particularly significant when viewed on a nationwide per capita basis, falls especially heavily on the comparatively small part of the population that is faced with heavy medical bills, and because of the peculiar nature of the business, in which the person who pays the bills has little chance to look out for his own economic interests since he has no choice over what to buy: the prescription is written for him by the doctor. This led Kefauver to open the hearings by announcing that so far as he was concerned his bill was a moderate one, involving changes in the ground rules as a result of which the pattern of competition in the industry would tend to move naturally in a direction more in keeping with the public interest. The alternative, Kefauver suggested, would be direct federal controls.

To conservatives the extra cost of drugs is not significant enough to warrant another step in the increasingly large role of the federal government in the economy. They are concerned that this legislation, aimed at a particular industry, would lead to demands to change the ground rules in other particular industries. This tendency suggests to many conservatives a more intimate degree of federal interference, as opposed to the bulk of the business regulatory legislation which has grown up since the turn of the century, which tended only to lay down ground rules for business competition generally. The AMA naturally finds itself sharing the views of the conservatives, not only because the leaders of organized medicine are themselves conservative, but because their greatest political interest is in opposing the development of socialized medicine, and they cannot help feeling, probably correctly, that any increase in the federal role in medicine weakens the resistance to a national health service. This may be especially true here, for the professed aim of the bill is to alter the circumstances that make the industry's heavy investment in promotion profitable. It would make the drug business less profitable, thereby reducing the economic power of a principal political ally of the AMA. It would, if it serves its purposes, sharply reduce the amount of promotion, and this would reduce the AMA's own resources, since the AMA, in fighting the increasingly expensive battle against a government-financed health service, has come to rely heavily on the money its journals earn from drug advertising. For all these reasons a far more intense controversy surrounds the bill than a casual reading of Kefauver's bill would suggest. For the bill, on a casual reading, appears to contain nothing more than a series of minor technical changes in laws of whose existence the public is scarcely even aware.—H.M.

News Notes

Micrometeorites

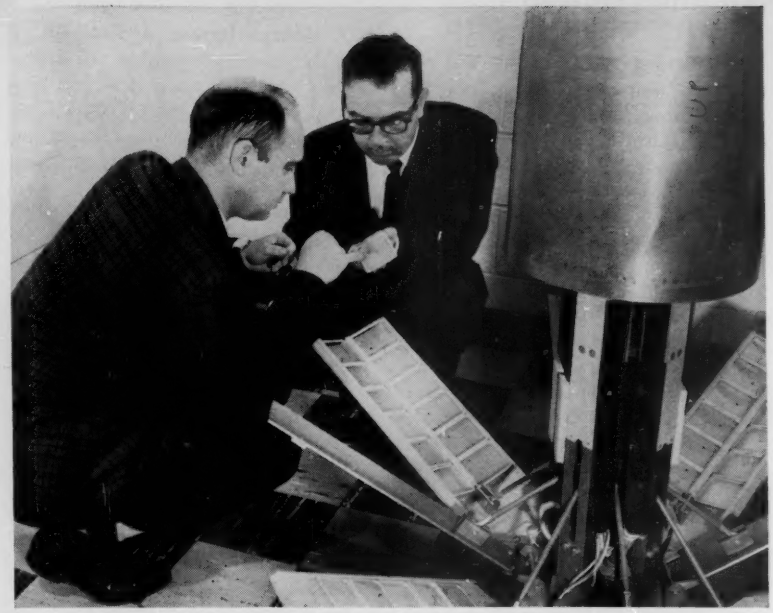
Three attempts were made recently by U.S. scientists to study micrometeorites, a potential hazard to manned space flight because of the damage they may cause to space vehicles on impact. The tiny particles move at speeds of over 47 miles a second.

The Air Force succeeded in collecting what may be the first micrometeorite samples with an Aerobee-Hi research rocket nosecone dubbed the "Venus flytrap." The particles were caught in plastic traps which were exposed as the cone opened when it reached an altitude of 47 miles. The exposure was maintained during the cone's ride up to 102 miles and was cut off at 65 miles as the cone returned to earth (see cut).

Scientists from the Air Force Cambridge Research Laboratories who examined the traps said the contents showed the existence of a dense band of micrometeorites which envelops the earth somewhere between these extreme altitudes. The traps were struck by ten particles per square centimeter each second.

Two types of micrometeorite detectors or traps were used: one made up of three physically separated layers of plastic, the two top layers of Mylar film 1/4000 and 1/1000 of an inch thick, respectively, and a ⅛-inch sheet of Plexiglas; another of relatively thick films of three harder plastics, Millipore, Formvar, and Lucite. The particles passed through the Mylar film layers, leaving holes, many visible to the naked eye. When they struck the Plexiglas, small craters, some also visible, resulted. Craters also were detected on the Lucite film, but most evidence of micrometeorite contact was apparent only through microscopic examination. Few micrometeorites themselves were collected since they apparently vaporized on contact with the detecting surfaces.

AFCRL scientists are interested in the residual bits of the space dust lining the walls of the craters in the plastic as well as in the meteorites themselves since it is believed the particles may provide new clues concerning the origin of the meteorites and, perhaps, the origin of the earth and the solar system. Complete anal-



Portion of the mechanism used to expose plastic traps carried in the nosecone of an Aerobee-Hi rocket which brought micrometeorite samples back to earth. Project scientists Thomas Ryan and Robert Soberman examine one of the traps. [Air Force Cambridge Research Laboratories]

ysis may take several years. It will be done for the most part by electron microscopy, which must be used because many of the particles to be examined are smaller than the wavelength of light. Study of one square inch may take a year; samples are being made available to interested and qualified scientists.

Other Shots

The Air Force followed up the "fly-trap" launch by sending up an acoustic rocket to measure the intensity of the sound of the impacts of the particles. Variations in sound intensity are recorded on tape and telemetered back to earth. These measurements will help pinpoint the altitude boundaries of the newly discovered micrometeorite band. They also will provide data that will permit a more accurate evaluation of how micrometeorite bombardment on a space vehicle may affect an astronaut. This sound has been compared with the sound of machine-gun bullets striking a metal surface. Since penetration of micrometeorites can be blocked by plastic surfaces, their damage potential may be more psychological in nature than physical.

The National Aeronautics and Space Administration tried and failed to launch a 125-pound satellite last week to measure the impact of micrometeorites on various metals. The experiment is part of a program to prepare the way for the safe orbit and recovery of an astronaut later this year. A malfunctioning rocket was behind the failure.

The attempted launch also was another test for NASA's Scout, the first multiple-stage, solid-fuel booster. The third stage failed to ignite. This marked the Scout's second failure in three trials. Nicknamed "the poor man's rocket," the Scout is being developed for use in various space experiments which do not require the larger thrust afforded by liquid-fuel rockets. Solid-fuel boosters are easier to handle and are considerably cheaper than the huge liquid-fuel boosters. Another try with the Scout to launch a micrometeorite satellite will be made in the near future, a NASA spokesman said.

Catch in Space

The sixth recovery of a 300-pound Discoverer capsule was made in the air this week after its 50-hour, 36-minute ride in space. Launched in a polar orbit from Vandenberg Air Force Base in California, the capsule was in the nose of the 25-foot Agena second stage of an 81-foot, 2450-pound booster, the 26th in the Discoverer series. Seven of the series have failed to orbit.

The kettledrum-shaped capsule was caught in the air on the first try by a two-engine C-119, half an hour after a ground signal had triggered its release from space on its 32nd orbit. Original plans were to have the capsule orbit for 4 days; it was called back, according to an Air Force spokesman, only because all data desired from the probe had been telemetered back. In the past, however, capsules have been recalled before completing the planned number of orbits because of loss of gas necessary for control. The time and number of orbits yield information on orbital speed, weight, mass, and ejection speeds important for planning for future recoveries.

The capsule contained the standard Discoverer package consisting of the elements iron, bismuth, yttrium, magnesium, nickel, lead, and titanium and, in addition, silicon. Silicon was included to measure the possible damaging effects of radiation on solar cells, which are a principal source of energy in many satellites. The Discoverer XXVI capsule, like all its predecessors, is gold-plated. Gold is used because it reflects heat and thus protects the capsule and its contents from possible damage from exposure to high temperature during the return to earth. It is also a good conductor of energy, and one of the scientific objectives is to measure the amount and effects of radiation.

Useful Debris

Left in the Agena still whirling in space are materials to measure cosmic and radio radiation and density of ions and micrometeorite particles. Particle density also is being measured by the erosion, by particle bombardment, of a tuned radio crystal which, as it is chipped away, will change its transmission frequency. The Agena also has a special radio receiver that transmits radio noise from space back to earth. This telemetered information is adding to knowledge of radio astronomy and will be useful in the development of communication satellites.

This is the first time extra experiments have been left in the remnants of a Discoverer shot. "Reliability of the Discoverer program has now advanced to the point where additional

equipment can be added for scientific experiments," an Air Force spokesman said.

Of the 19 Discoverers that have been put into orbit, 15 have carried recoverable capsules. Discoverer XIII was the first successful space catch.

The **Atomic Energy Commission's tunnels** in the Cactus Mountains of Nevada are ready for underground nuclear tests for peaceful or military purposes once an official go-ahead is given. On 30 Oct. 1958, a Hiroshima-size bomb was set off underground in these AEC tunnels. The next day the tunnels became inactive as a result of the gentlemen's agreement to suspend nuclear tests reached by the United States, the Soviet Union, and Great Britain. Since then, however, tunnel development has continued, explosion debris has been cleared away, and enlargements and improvements such as air-conditioning, lighting, and railways have been added.

Atomic experts in Great Britain are designing instruments to detect nuclear tests in space, it was reported in the British Atomic Energy Authority annual report. It should be possible to detect such explosions at distances over 625,000 miles under proper atmospheric conditions, the report said. Work also is being done in seismic research to improve the ability to distinguish between underground explosions and earthquakes.

The headquarters of the Royal Society, Great Britain's **space phone center**, set up to relay telephone conversations around the world from signals bounced off of a system of communication satellites, has been unable to get a local line. The society has to wait its turn, it was told by the telephone company. It is now half-way down a long waiting list.

Export to Czechoslovakia of 25 millicuries of carbon-14 and 100 millicuries of tritium has been approved by the Atomic Energy Commission for use in medical and biochemical research. The AEC said the materials would not be of military value.

The **United States and Poland** have signed a $115,000 agreement to provide Polish medical students and physicians with inexpensive translations of standard American medical textbooks.

Announcements

A World Academy of Art and Science has been organized to "function as an informal 'world university.' " The academy states its fundamental aim is "to rediscover the language of mutual understanding . . ." and, "with the help of science and the support of all cultural forces of mankind," it hopes to "serve as an impartial and unpolitical adviser, complementing other organizations . . ." and to contribute in "leading mankind to an era of true progress, true human welfare, and true happiness." Officers of the new academy are:

Lord John Boyd Orr, chancellor of the University of Glasgow, president.

Hermann J. Muller, professor of zoology, Indiana University, vice president.

Hugo Osvald, retired professor of botany, Royal Institute of Agriculture, Uppsala, Sweden, vice president.

Hugo Boyko, ecological adviser to the National Research Council, Prime Minister's Office, Israel, secretary general.

The first volume of the academy's publication series, *Science and the Future of Mankind*, is being published by W. Junk, The Hague, Netherlands. (Hugo Boyko, WAAS, 1 Ruppin St., Rehovot, Israel)

The placement service of the American Phytopathological Society has names and qualifications of candidates available for employment in **plant pathology**. The service is free to members and is available to any employers with vacancies. (Phytopathology Placement Service, Crops Research Division, Plant Industry Station, Beltsville, Md.)

A booklet containing a survey of existing data on the use of **radioisotopes and radiation sources**, with a report by a panel of medical physicists and radiotherapists, has been published by the International Atomic Energy Agency, Vienna. A limited number of copies of *Therapeutic Dose Distributions with High-Energy Radiation* are available free of charge for scientific reviews or discussions in the press. (Division of Public Information, IAEA, Vienna 1, Austria)

The International **Atomic Energy** Agency is seeking scientific advisers for assignments in foreign countries in connection with the technical assistance program. Positions are for three, six, and twelve months. (IAEA, Vienna I, Austria)

Scientists in the News

J. George Harrar, agricultural expert and a vice president of the Rockefeller Foundation since 1959, has been elected president of the foundation. He succeeds Dean Rusk, who resigned last January to become Secretary of State.

Ephraim Katchalski, head of the biophysics department at Weizmann Institute of Science, Rehovot, Israel, has been awarded the 1960 Rothschild prize for his work on the structure of polyamino acids.

Marvin L. Sears, of Johns Hopkins Hospital, has been appointed the first full-time chief of the section of ophthalmology at the Yale–New Haven Medical Center.

Harry D. Holmgren, of the U.S. Naval Research Laboratory, has been appointed associate professor of physics at the University of Maryland.

Recent appointments to the faculty of the New York University Schools of Medicine:

Joseph Ransohoff, Columbia University College of Physicians and Surgeons, will become professor and chairman of the department of neurosurgery.

Valentino D. B. Mazzia, Cornell University Medical College, will become professor and chairman of the department of anesthesiology.

Milton Eisler, former senior scientist in Schering Corporation's research division, has been appointed president and laboratory director of Probio, Inc., in Nyack, N.Y., a newly formed company which produces biologicals for laboratory use.

Louis C. Zopf, dean of the State University of Iowa's College of Pharmacy, has received the 1961 E. R. Squibb and Sons distinguished service award.

Erratum: In the report "Formation of diamond by explosive shock" [*Science* **133**, 1821 (9 June 1961)], by P. S. DeCarli and J. C. Jamieson, the unit of measure given in line 4 of the last paragraph in column 2, page 1821, should have been degrees of geometrical angle rather than temperature.

Erratum: In the news note, "Space discoverer recovery," on page 2002 of the 23 June issue, the statement in the 4th paragraph (lines 6 and 7) that the Discoverer program achieved "the first successful orbit and recovery of animals" is wrong. The statement should have been omitted, and the following sentence should have concluded the paragraph: "The Discoverer program also marked the first attempt by the United States to put animals in orbit."

Guide to Biological Horizons

Is this volume an authoritative source book, or does it have handicaps that make it useless?

Mark Graubard

To the publisher's descriptive phrase, "A unique achievement in one volume," and the introduction's comment, "the Editor realizes that it is impossible to please everyone" (both statements are fully justified), should be added the plaint, "the book is also a reviewer's nightmare." There can be no doubt that there was a crying need for just such a convenient and authoritative encyclopedia, one that was both expansive and up to date. **The Encyclopedia of the Biological Sciences** (Reinhold, New York, 1961. 1119 pp. $20), edited by Peter Gray, is remarkably successful for fulfilling so demanding a challenge. It could hardly be otherwise with the adopted editorial policy of having only recognized and salient experts in various fields discuss the basic or pivotal terms and concepts in the entire range of the biological sciences. The coverage is enormous and the topics are keenly stimulating to the relaxed browser—witness the first and the last six entries: Abiogenesis, Acantharia see Actinopoda, Acanthocephala, Acarina, Acoelomata, Actinomycetes; and then Wöhler, Friedrich (umlaut omitted), Wood, Xiphosura, Xylem, Zingiberales, and Zoogeography. The people writing the compact, well-edited, and in general, excellently styled articles are men of the caliber of Beadle (biochemical genetics), Davson (secretion), Oparin (origin of life), Romer (Chordata), Waksman (Actinomycetes), Williams, R. J. (biochemical individuality)—to pick at random a few of the generally better known names from the vast list. Needless to add, every one of the more than 600 contributors is a scientist of stature writing in his own specialized field in which he cannot be found wanting, no matter how firmly one may disagree with one point or another in his approach, coverage or stress.

As a rule, wherever needed, excellent illustrations are used. In most respects the index is adequate and generous, all articles seem to contain a goodly supply of cross references and to carry in their bibliographies the very latest and best lists of suggested titles as sources for more detailed information. But, above all, the science of biology is brought up to date in its modern, lush, and variegated splendor, with the newest terms, concepts, and pathways mustered for review. A biologist who completed his formal training even 20 years ago, but, perish the thought, has not kept abreast of events that are moving at full speed, may very likely find himself, perhaps on the third page, in the plight of Rip Van Winkle.

After having said all this, however, I feel obliged to add, in all honesty, the reactions of two equally, if not better, qualified fellow workers in the vineyard. One is an older man, a competent teacher, modest and studious; the other is considerably younger but clever, erudite, outspoken, and keen. The former was delighted with the volume, read it avidly for 5 days on end, and hated to part with it. The *Encyclopedia* fulfilled all his expectations, and more. It brought to his desk the entire panorama of modern biology: the most recent researches, experiments, and concepts which he would not otherwise have encountered in his own limited subject, an area in which his own work is fairly conspicuous. He read, he declared, with an avidity he had not experienced in many years about how whale pups come into the world, of the involvement of ATP (adenosine triphosphate) in the growth of the microfibrils of cellulose, of the endoplasmic reticulum under "Cell," of melanophore-expanding hormones, as well as of grassland climates, population genetics, the gradient of starch grain density in the *Lycopodium* embryo, hibernation and mere stupor, and RNA (ribonucleic acid) synthesis, of course. What a package of relevant knowledge between two covers. Although in spots the *Encyclopedia* made him feel a bit inadequate, he got a thrill out of discovering at least one serious miss—the term *estivation* is not cited. He consoled himself with "Excretion," and that was excellent.

The younger man, on the other hand, bluntly declared with unconcealed contempt that he would not recommend the *Encyclopedia* to high school teachers, to graduate students, or to colleagues because the book had enough shortcomings to be disqualified on all these fronts. Needless to say, he had some valid criticism supported by evidence and corroborated by a few other readers. Thus, he feels that such major items as crossing over or synapse, though mentioned in the index, are given peremptory and inadequate treatment, not in accord with their true status in modern science. Neurosecretion is poorly used in the index and inadequately treated, and cytoplasmic inheritance is omitted. In response to the plea that, granting the particular failings in the index, all these topics are fairly well covered by integrating brief references in several articles—articles which the reader would naturally consult in the course of his search—quite a few other objections of the same nature were promptly advanced to support and uphold the original condemnation. Nevertheless, it is a fact that Sonneborn's article on "Plasmagene" entails cytoplasmic inheritance and that the one on "Impulse conduction and transmission" by A. S. Marazzi deals with the synapse, although neither reference is listed in the index.

Summary and Verdict

These and other comments lead to the following: The editor's dictum that no work of this kind can please everybody is correct. Also, some shortcomings in such a pioneering work seem inevitable, as they can probably be found in the most pleasing of brides. One serious weakness is inherent in such a work: Precisely because outstanding authorities are called upon they are likely to stress their own researches and may overlook the contributions or approaches of others. This seems to be

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a frequently encountered human factor, and it may be a hard one to eliminate. Next, the editor may regard a certain topic well enough covered in one or two articles not to plan for a separate heading, since neither size nor space is unlimited. The editor, no doubt, has to curb many an author who understandably might be carried away with enthusiasm for his own subject. But on the whole the space allotment seems fair, with precision and compactness the general rule. Since judgment is difficult, here are some examples: Carbon dating, 3¼ columns; coloration of animals, 13 (this includes three columns of various chemical formulas); endocrine system, 9; plastid, 3⅓; pineal, 1; endogenous rhythms, 2; photoperiodism (plant), 3½; genetic drift, 2; salt marsh, 2; primates, 9; population genetics, 9 (including all major equations).

While the idea of including biographical sketches is a valuable and pleasant diversion in a volume of this kind, the inclusion of such names as Agnes Arber, but not C. B. Bridges or E. B. Wilson, presents a problem. Moreover, many of the historical sketches are quite superficial and faulty. Entirely false and even expendable is the paragraph on Giodanao Bruno; Wöhler did not synthesize urea but found it in the reaction system; Johannes Müller's somewhat flippant biographical sketch lacks the spirit of that great man.

However, all factors considered, the verdict remains as originally stated. The volume is an excellent pioneering venture of immense value to every teacher and student of biology. It is thorough, authoritative, up to date, and it is exceptionally strong in reporting the latest researches in most fields of biology. It is beautifully illustrated, well cross-referenced and indexed (with minor lapses here and there which should be corrected in revision) and with more-than-hoped-for coverage. The style is so lucid that any alert high school student can consult most entries with profit. Such a student may find quite a few wholly incomprehensible because they presuppose considerable knowledge of chemistry, physics, and mathematics. But these provide references to fuller texts; besides, if he goes so far as to seek out these references, he may be able to plough through with some profit. Even the hard ones give him the opportunity to do so.

And all this in one volume—and at a relatively tolerable price for such an enterprise.

Two Congos

Congo. Background of conflict. Alan P. Merriam. Northwestern University Press, Evanston, Ill., 1961. xiii + 368 pp. Illus. $6.

Alan Merriam, an anthropologist at Northwestern University, has been in the Belgian Congo for extensive research visits on two occasions: in the early 1950's, when the Congo was still regarded by many as the "model colony," and in 1959 and 1960, during the transition to independence and, as it turned out, chaos. From this personal background and from a wealth of detailed information garnered from many diverse sources, he has written a book which, though focused on events that have not yet run their full course, provides an overview valuable not only for an understanding of what the Congo is like now but also for an understanding of the kind of stage upon which future events will unfold.

The volume begins with a short introduction that considers historical, geographic, and ethnographic matters and then turns directly to Belgian colonial policy whose guiding principle of paternalism, with the usual colonial components of cupidity intricately interwoven with a measure of sincere but prideful and insensitive idealism, serves to explain much of the background out of which later events grew, swiftly, disastrously, and yet, as Merriam makes clear, not really inevitably. One of the most interesting chapters describes, in concretely human terms, how independence came to two "Congos" (all too often only one or the other is talked about in isolation): the Congo of the interior (in this case, the village in which Merriam resided during most of his field research) and the Congo of the urban center (Stanleyville being the example used). After these descriptions, the detailed, more purely political narrative of parties, leaders, negotiations, and the vicissitudes of pre- and post-independence politics becomes more understandable to the reader, more consistent in its apparent lack of logic. Merriam has happily chosen to present many of these facts in the framework of a calendar of specific events. With the feeling of immediacy that it gives, this calendar will remain invaluable in any future discussion of the series of Congolese debacles, for already the accidental is too often forgotten and the small but crucial event tends to disappear as sweeping mythologies, always so appealing in their simplicity, begin to take shape. There is a sobering aspect to this retrospective view; if the Congolese villager and townsman are found to have been unrealistic in their expectations, so are many of the supposedly more sophisticated analysts—on one side, the Belgians and the apologists of the "perfect colony" who were blind to the dynamics of a continent which they forgot existed at all; and those on the other side who, fascinated with general trends, impatiently ignored the role of the unique and concrete fact and hailed the hasty Belgian capitulation as a show of political realism.

Mercifully, the reports from the Congo have left the front page in recent weeks. It would, however, be unforgivable for us to slip once again into forgetting that the Congo exists. This book will amply prepare the reader to avoid this error; and it will prepare him not only to expect more news but also to understand the news better when it does come.

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California Flora

Flora of the Santa Cruz Mountains of California. A manual of the vascular plants. John Hunter Thomas. Stanford University Press, Stanford, Calif., 1961. viii + 434 pp. Illus. $8.50.

The Santa Cruz Mountains of California form the backbone of the peninsula west of San Francisco Bay and north of Monterey Bay. Although the range is only about 50 miles long and 2000 feet high, the flora is rich and varied. The mountains dip down into the ocean on the west, and the flora is coastal. Above the beaches and cliffs are extensive areas of redwood forest (Pacific Forest). This vegetation type occurs also in the more moist canyons on the east slope of the range, but most of the drier inland side is covered by California Chaparral. The inland foothills are California Oak Woodland. Thus the flora of the Santa Cruz Mountains includes a high percentage of the species occurring in the lowlands of northern California.

The text includes distributional notes, keys to the families, genera, and species, some synonymy, and intro-

ductory description of the mountain range and of adjacent areas from the standpoint of geology and climate as well as of vegetation types.

This is a useful local manual which is well prepared and which will be especially valuable for botanists and others in the region who wish to key out quickly the local species. For this purpose, the relatively simple keys should be useful, but they are oversimplified for application to the flora of the state as a whole. Statements of geographical distribution of species are restricted to the Santa Cruz Mountain localities, and the reader is referred to other works for general distribution.

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Boolean Algebra

Boolean Algebra and Its Applications. J. Eldon Whitesitt. Addison-Wesley, Reading, Mass., 1961. x + 182 pp. Illus. $6.75.

This is a text for a one-semester college course presupposing only a limited mathematical background. The course could be for either good engineering students or practically inclined students of mathematics.

In chapter 1 Whitesitt develops the algebra of sets intuitively from Venn diagrams, discovering the basic properties of complementation (denoted by $'$), union (denoted by $+$), and intersection of sets (denoted by $\cdot$ or juxtaposition). In chapter 2, Boolean algebra is formalized from minimal postulates. The Stone representation theorem—that every abstract Boolean algebra is isomorphic to an algebra of sets—is stated but not proved. In chapter 3 the author treats the algebra of propositions in symbolic logic. He occasionally goes beyond Boolean algebra to discuss quantifiers and rules of inference. But the basic theme is the use of Venn diagrams and the formal simplification of propositional functions.

Chapters 4 to 6 are on the engineering side. After showing the use of Boolean algebra in series-parallel circuits, the author treats more complicated circuits, showing how to reduce them to series-parallel form. The design of n-terminal, double-contact switching circuits is discussed lightly. Next one reads of sequential relay circuits and, in chapter 6, of half-adders, adders, and even parallel multipliers for digital computers. Chapter 7 discusses probability in finite sample spaces.

There are many illustrative examples, exercises for the reader (many involving complicated verbal puzzles to be untangled), and about half a dozen references at the end of each chapter. Answers to selected problems are provided at the end of the book.

I found the book very readable and informative. In addition to the applications, many important mathematical ideas arise naturally and simply in this subject (for example, duality, isomorphism, function), and these might justify such an off-beat course in a modern mathematics curriculum. But, on balance, for mathematics students the book and the subject appear better suited for self-study. I cannot judge the book as an engineering text.

The author's definition of a function (page 33) as an expression cannot be condoned in 1961. I was surprised to find so little use of the Karnaugh-Veitch diagrams which are so popular among engineers.

A closely related book is Franz E. Hohn's *Applied Boolean Algebra, an Elementary Introduction* (Macmillan, New York, 1960).

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Relativity for the Layman

What Is Relativity? L. D. Landau and G. B. Rumer. Basic Books, New York, N.Y., 1961. vi + 72 pp. Illus. $1.95.

This book, which is being published in Basic Books' Science and Discovery Series, is a translation from the Russian, the authors being well-known physicists of the Soviet Union. The translator, N. Kemmer, is himself an internationally known British physicist. With this formidable authorship, the book is a charming exposition of the basic principles of the special theory of relativity, intended for the youthful lay reader and enlivened with some 20 freehand sketches, some of them amusing, all instructive. The scope covered by this brief presentation is strictly limited; it is confined to a thorough conceptual exposition of the foundations of the theory, a discussion of the kinematic effects of special relativity, and an explanation of the variability of relativistic mass. The authors have avoided the use of even the simplest algebra; but they do use arithmetic calculations to illustrate their qualitative arguments. Nevertheless, the book is penetrating, rather than descriptive, and makes demands on the intellectual capabilities of the reader. It can be warmly recommended not only to high school students but also to college students who are not primarily science-minded.

The publishers are to be commended for having held the price down to a nonrelativistic level, even though they have provided the volume with a standard hard cover and a tastefully designed dust jacket.

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Econology

Bargaining and Group Decision Making. Experiments in bilateral monopoly. Sidney Siegel and Lawrence E. Fouraker. McGraw-Hill, New York, 1960. x + 132 pp. Illus. $4.90.

This book is one of the fruits of the interdisciplinary tree and one that may be equally palatable to both of the disciplines involved, namely, economics and experimental social psychology. It was awarded the Monograph prize of the American Academy of Arts and Sciences for 1959 in the social sciences. The authors point out that economics is the most advanced theoretically of the social sciences, while psychology is the most advanced in rigorous empirical methodology. The marriage of the strong aspects of the two disciplines has produced what appears to be a viable hybrid (econology?) consisting of explicit hypotheses for the psychologist to test and resulting modifications of theory for the economist to encompass and expand.

The experimental technique designed to test deductions from economic theory is simple and elegant. Pairs of college students were provided with isoprofit tables describing precisely various profit levels (in real money!) attainable and the prices and quantities of product X to be exchanged in order to reach certain levels of profit. The result of the ensuing bargaining between buyer and seller is that each goes home with the amount of money he decides is his largest possible profit. Bargaining is

done in isolation by passing numerical price and quantity bids back and forth via the experimenter until the contestants are satisfied with the bargain achieved.

The hypotheses tested by these laboratory experiments centered around the case of equal bargaining strength, the theoretically indeterminate case. The main hypothesis, that contracts negotiated under simulated, bilateral, monopoly conditions will tend to the quantity which maximizes joint payoff, was confirmed. By varying cost and revenue functions, the generality of the result was established. It was further shown that personal characteristics of the bargainers enter heavily into the determination of differential payoff and price. The variability of contracts around the maximum joint payoff appears to be controlled by the amount of information the bargainers have. Results are reported for the complete-complete, incomplete-complete and incomplete-incomplete information cases.

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Third Ur Kingdom Archives

Sumerian Economic Texts from the Third Ur Dynasty. A catalogue and discussion of documents from various collections. Tom B. Jones and W. Snyder. University of Minnesota Press, Minneapolis, 1961. 421 pp. Illus. $10.

Administrative and economic texts from the archives of the third Ur kingdom (end of the 3rd millennium B.C.) already published are approaching the 15,000 mark, but a large number in public and private collections all over the world remain unpublished. And, of course, complete archives from the same period are probably still buried in the sands of southern Iraq. This extraordinary wealth of source material, unmatched by that of any other period of antiquity, is nevertheless difficult to digest: the large number of texts, the dispersion of the publications (some of them rather inadequate), the large amount of necessarily tedious preparatory work, and last but not least the language difficulties have until now prevented the preparation of a reasonably complete synthesis useful to historians of economics and technology.

The present volume represents a contribution towards that goal, without intending to be in any way a complete exposition of the available material. The catalog comprises 354 new pieces, most of them from the collection of the Rosicrucian Egyptian, Oriental Museum in San José, California; the others are from eight or nine different public and private collections. The texts are given in transliteration only, except for a few copies of difficult cuneiform passages. A good deal of attention was given to presenting the individual texts as clearly as possible (see, for example, the tables accompanying No. 78). The commentary consists of 11 independent chapters on selected points touching not only on the texts presented by the authors but also on questions arising from the whole corpus concerned with the third Ur dynasty; the reconstruction of the prosopography and administrative frame of Drehem will be specially welcome for future research. A useful bibliography, intended to supplement the one given by Oppenheim in his catalog of the Eames collection (still the most informative and well-balanced work in this field), and comprehensive indexes complete the book.

However the synthesis of all Ur III material is yet to be made, and basic questions remain unanswered: Is the available material a representative sample of the economic life of the period? Which sectors of this economic life are represented and which are excluded? As is true of all reconstructions, we must first study carefully the limitations of our material to avoid unjustified extrapolations and the abuse of the arguments *ex silentio*.

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Computer Technology

Digital Applications of Magnetic Devices. Albert J. Meyerhoff and others, Eds. Wiley, New York, 1960. xix + 604 pp. Illus. $14.

In the computing industry the magnetic core has become the accepted device for large-scale storage of information because of its high reliability even under adverse conditions, its high speed capabilities, and its low energy expenditure. Most of the cores in digital computer systems are used for high-speed memory; however, they are also employed as logical circuit elements. The present text is mainly devoted to the latter applications. Much of the material is available in appropriate journals in less complete form; some of the topics have been considered in more general texts, but not as comprehensively as in this treatment. The editors have performed a very useful service in providing a one-volume, systematic treatment of an important field of digital technology.

The book, a reference text in the field of digital magnetic circuits, emphasizes the utilization of magnetic core circuits in the implementation of logical functions in digital systems. Although it consists of chapters written by 25 active workers from six industrial organizations, the volume is a well-organized and well-edited, unified presentation. Following the first part which discusses the fundamentals of magnetic core circuit technology, the six remaining parts cover particular areas of application. Each part consists of an introductory chapter explaining the general philosophy of the devices under consideration and of chapters discussing detailed circuit design, logical design, and systems design. Many references are cited, and the index is well prepared and complete.

The treatment of subject matter is, on the whole, clear and understandable. The section devoted to magnetic core memories is limited in scope to systems design. The editor justifies his position by stating that the existing literature covering this area is more extensive than that covering the topics he chose to elaborate on, but I feel that more could have been written here. The book should provide the digital systems designer with a set of digital techniques which have proven to be useful and reliable.

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Reprints

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Reports

Lead-210 in Natural Waters

Abstract. The distribution of lead-210 which enters the oceans subsequent to its production in the atmosphere by radon-222 decay, shows an increase with depth in sea water. By use of a simplified two-layer model of the ocean, a residence time of lead in the upper mixed layer of less than 2 years is derived. It is suggested that the marine biosphere is responsible for the conveyance of lead from surface to deeper waters. The distribution of lead-210 in the Colorado River indicated a rapid removal along the path from its origin in the feed waters to the reservoir at Lake Mead.

A recent series of papers (*1*, *2*) illustrating the use of lead-210 as a tracer of natural processes in the atmosphere and on the earth's surface prompted us to investigate the distribution of this isotope in natural waters. The present picture of the behaviors of lead-210 and its precursor radon-222, in the uranium-238 decay series, can be summarized in the following way. Radon-222 escapes from the surface rocks at an average rate of 42 atoms per minute per square centimeter of land surface (*3*) into the atmosphere, where it decays with its half-life of 3.8 days. The average standing crop of radon in the atmosphere therefore should be about 42 disintegrations per minute per square centimeter (or 3.3×10^5 atoms/cm^2) of land area.

The radon nuclei transform through a series of short-lived daughters to lead-210 with a half-life of 21.4 years (*4*). This long half-life would permit a uniform distribution of lead-210 to be approached in the atmosphere. However, this condition is never realized since the removal of lead-210 by natural precipitation effectively limits its residence in the atmosphere to a few weeks (*1*). This period, though short, is nevertheless long enough to allow a considerable amount of lead-210 to be transported in the atmosphere over the oceans where it is removed by rains. Since the land area represents but one-third of the total surface area of the earth, the average production rate of lead-210 should be 42/3 or 14 atoms per minute per square centimeter of earth's surface. The observed fall-out rate of lead-210 agrees well with this value. The concentrations in rains over continents and oceanic islands vary about 5 disintegrations per minute per liter or 8×10^7 atoms/lit. (*1*, *5*). This is equivalent to a fallout of 15 atoms per minute per square centimeter of earth's surface, if one assumes an annual rainfall of 1 m.

It was initially felt that this unsupported lead might be a useful tracer for studying the mixing between the upper mixed layer and the deeper waters of the ocean, a process that is presumed to take place in a time of the order of or less than the half-life of lead-210. A rainfall of 1 m per year into a mixed layer of 100-m depth should result in an input of lead-210 of 0.5 disintegration per minute per square centimeter per year (0.05 disintegration per minute per liter of water in the mixed layer per year). The production of lead-210 in the mixed layer from the dissolved radium-226 is comparatively small. A concentration of 4 to 5 $\times$ 10^{-14} grams of radium per liter produces lead-210 at a rate of 0.003 disintegration per minute per liter per year. If no transfer of lead-210 takes place between the mixed layer and the water below the thermocline, the equilibrium value of lead-210 should be $(0.05 + 0.003) \times 21.4/0.693 = 1.6$ disintegrations per minute per liter.

It may be noted that the input of lead-210 from the atmosphere is 17 times the amount resulting from radium decay in the mixed layer but is only about 10 percent of the amount that results from the decay of radium in the entire ocean.

A simple and effective technique for the separation with known yield of lead-210 from bismuth-210 and other radionuclides in natural waters was devised. To a membrane-filtered water sample of about 20 liters, 30 mg of lead carrier, as lead nitrate free of any lead-210, was added. The lead was then precipitated as lead chromate by the addition of sodium chromate. The chromate precipitate was dissolved in 1.5*N* HCl and passed through an anion-exchange column (AGI-X8, 100 to 200 mesh, analytical grade, from Bio-Rad Laboratories, Richmond, Calif.). The lead was eluted from the column with distilled water and reprecipitated as the chromate. The precipitate was dried to constant weight, which gave the chemical yield of the extraction process, and then deposited on planchets for radioactive assay under a low-level beta counter (background 0.07 count per minute and an efficiency for counting the bismuth-210 betas of about 34 percent). The lead-210 activity was determined and identified by measuring the growth of bismuth-210 in the sample.

The organic material from the biological tows and water filters was destroyed in a mixture of nitric and per-

Table 1. Distribution of lead-210, in disintegrations per minute per liter, in natural waters.

Sample	Lead-210
Ocean waters	
La Jolla Pier, 3 Nov. 1960	0.12
31°10′N, 120°54.5′W, 4200-m depth	
Surface water	0.10
600-m water	0.12
2000-m water	0.28
Biological material from tow No. 1	1.5×10^{-7}
Biological material from tow No. 2	7.5×10^{-7}
Rainwater	
Friday Harbor, Wash., 6 May 1960	0.8
La Jolla, Calif., 3 Nov. 1960	7.1
San Diego, Calif., 7 to 8 Dec. 1960	1.9
Snow	
Echo Lake, Colo., 13 Dec. 1960	
Feed water to Colorado River	3.8
Colorado River water	
Fruita, Colo., 14 Dec. 1960	14.7
Green River, Utah, 14 Dec. 1960	1.0
Hoover Dam, Lake Mead, 15 Dec. 1960	0.29
Miscellaneous	
Tap water, La Jolla, Calif.	0.12
Distilled water (blank run)	<0.01

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to contributors" [*Science* 125, 16 (1957)].

chloric acids. The residue from this treatment was taken up in 1.5*N* HCl and treated in the same manner as the water samples for the isolation of the lead-210. There was no lead-210 activity on the filters, within experimental error. The activity in the biological tows, comprised of zooplankton, was easily measurable, but was insignificant when considered on a per-liter-of-seawater basis.

The results of our work are given in Table 1. The over-all experimental errors in the tabulated values are less than 10 percent.

The activity in the oceanic mixed layer proved to be less than it was in deeper waters—a result contrary to expectations. This strongly suggests a removal of lead-210 from the surface waters to deeper water by biochemical or inorganic processes. This can be seen more clearly by setting up the steady-state equations for a simple two-layer model of the oceans (*6*):

$$dN_m/dt = 0 = P - BN_m - K_{m-d}N_m + K_{d-m}N_d - \lambda N_m$$

where N_m and N_d are the amounts of lead-210 in the surface and deep waters, K_{m-d} and K_{d-m} are the rate constants for the mixing of mixed to deep waters and deep to mixed waters, B is the rate constant for the biological or inorganic removal of lead, λ is the decay constant of lead-210, and P is the total input of lead-210 into the mixed layer both from atmospheric radon-decay and from radium-decay in the sea water. Rearranging, we find

$$P = (B + \lambda) N_m + (K_{m-d} N_m - K_{d-m} N_d)$$

Taking the volumes of the mixed and deep layers as 10 and 500 lit./cm^2 (that is, an average oceanic depth of 5000 m) respectively, and the concentration of lead-210 in the mixed and deep layers as 0.1 and 0.3 disintegration per minute per liter, we find

$$0.53 \frac{\text{disintegrations/min}}{\text{cm}^2} \text{ year}$$

$$= (B + 0.03)\ 1 + (K_{m-d} \times 1 - K_{d-m} \times 150)$$

$$\text{or } 0.50 = B + (K_{m-d} \times 1 - 150\ K_{d-m})$$

Although order of magnitude values of K_{m-d} and K_{d-m} exist (*6*), we first consider the extreme case where no mixing occurs between the mixed and deep layers, that is, $K_{m-d} = K_{d-m} = 0$. Here, B is 0.5, or the biological removal time of lead-210 is 2 years. The second term in the last equation must be negative for the cases where the K's have positive values, inasmuch as any physical mixing can result only in a net transfer of lead-210 from the deep to the mixed layer. This would make values of the biological removal period even smaller. However, the period may be longer, if the oceanic rains are, on the average, poorer in lead-210 than we have indicated. Nonetheless, the order of magnitude is of primary significance.

The residence time of lead in the deep oceans before precipitation to the sediments is of the order of 10,000 years (*7*). The markedly shorter residence time in surface waters emphasizes the distinction between the mechanisms of transport of lead from the mixed to the deep waters and from the deep waters to the sea floor. The well-known enrichment of heavy metals in the marine biosphere, coupled with the biological activity in the mixed layer, suggests biological transport in the first case, while inorganic processes are undoubtedly responsible for the accumulation of lead in sediments. The observations on the distribution of barium in the oceans (*8*) have already indicated the importance of biological activity in the conveyance of heavy metals from the mixed to deeper waters.

The very long residence time of lead in the deep oceans indicates that only an insignificant fraction of the oceanic lead-210 will be deposited in the sediments. This seems to be borne out by our observations also. The concentrations of lead-210 in deep-sea waters are found to be essentially in secular equilibrium with the radium-226 values reported for such waters (*9*).

The behavior of lead-210 in terrestrial surface waters was sought in order to evaluate its use as a tracer of the movements of these waters. It is quite clear from Table 1 that there is a rapid depletion of lead-210 in the Colorado River during its journey from the area of its feed waters to the man-made reservoir Lake Mead. These results clearly direct one to the conclusion that the composition of river waters reflects not only the geology of the drainage basins and the accompanying weathering processes therein but also, and possibly of equal significance, the chemical reactions, either inorganic or biochemical, that occur within these waters (*10*).

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15 March 1961

Discharge Patterns of Neurons in Cochlear Nucleus

Abstract. Patterns of discharge in slowly adapting, spontaneously discharging neurons of the cochlear nucleus were studied. A technique for analyzing the distribution of intervals between discharges of neurons is described. The response to a steady tone generally was an irregularly spaced train of impulses. In the majority of cells examined, the intervals between discharges were distributed exponentially. The mean interval and standard deviation of the distributions decreased as the level of afferent excitation was increased, but the modal value of the distribution was unchanged.

Many neurons of the mammalian central nervous system have highly irregular patterns of discharge. Measurement of the average frequency of discharge of these neurons does not sufficiently characterize their behavior. A useful method of analyzing the behavior of these neurons is to determine the frequency of occurrence of the various intervals at which they discharge. These intervals can be plotted in the form of a histogram. Histograms of this type have been constructed by various authors for muscle spindle receptors (*1*), retinal ganglion cells (*2*), and neurons of the auditory cortex (*3*). Analysis of these histograms may provide information about fundamental properties of the neuron (*1*, *2*, *4*). The present report is concerned with describing some examples of histograms of discharge intervals in units in a sensory nucleus in the cat.

Tungsten microelectrodes with tip diameters of 1 μ were used for the extra cellular recording of discharges of single neurons. Light pentobarbital anesthesia or awake chronic preparations with implanted microelectrode

advancers were used. Only spontaneously discharging neurons that adapted slowly to steady stimulation, and whose discharge characteristics were stable, were studied. Discharges were recorded on magnetic tape. Time intervals between discharges were electronically sorted by a machine constructed from standard digital elements. The machine contained a 100-kcy/sec oscillator that was used to measure the discharge intervals by counting the number of oscillator cycles that occur between successive discharges of the neuron. A logic network was used to determine when a count fell between the limits of a particular predetermined class interval. A bank of registers totaled the counts for each class interval (*5*).

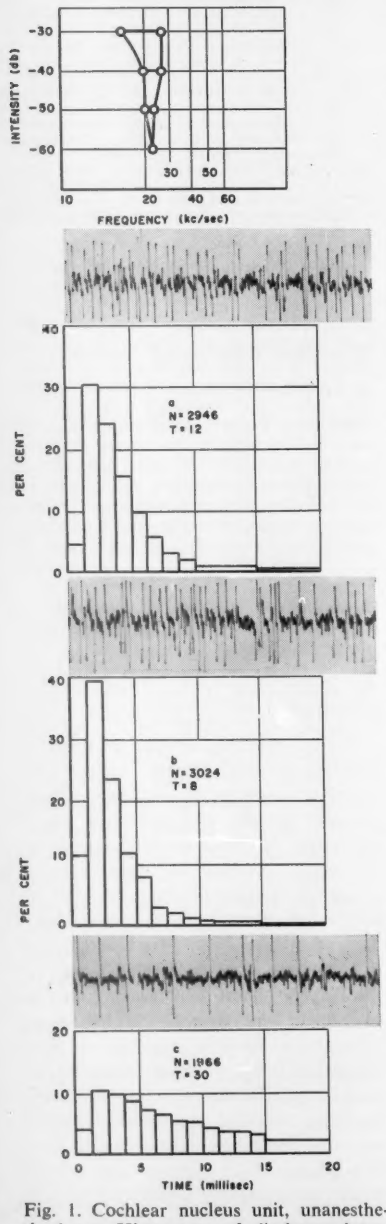

Fig. 1. Cochlear nucleus unit, unanesthetized cat. Histograms of discharge intervals: *a*, stimulation of ipsilateral ear with a tone of 21.5 kcy/sec at −20 db; *b*, stimulation with a tone of 21.5 kcy/sec at −40 db; *c*, no stimulus, spontaneous activity. The exponential tails of these histograms have been omitted to conserve space. Insets: Threshold of response versus frequency. Oscillographic strips: Recordings of the electrical activity of the neuron for a 1/10-sec period. (*N*, total number of discharges; *T*, approximate length of record in seconds)

Histograms of discharge intervals were obtained for 31 cells in the cochlear nucleus, making use of a class interval of 5 msec. Thirty of these cells had an exponential distribution of interspike intervals that could be approximated by the equation:

$$P(t) = re^{-rt}$$

where $P(t)$ is the probability density for intervals of duration t, and r is the mean frequency of discharge. To obtain a finer structure for the histograms, discharge interval distributions were also obtained with a class interval width of 1.25 msec. A histogram for a typical unit is shown in Fig. 1. This unit responded to high-frequency tones and had a click latency of 2 msec at a sound intensity level 40 db above threshold. Without stimulus the cell had a mean discharge rate of 73 pulses per second. The standard deviation of the interval distribution was 13.6 msec. With a sustained tone having a level of −40 db (20 db above threshold), the average discharge rate of a cell was 303 pulses per second, and the interval distribution was narrower, with a standard deviation of 2.2 msec. With an increase in the strength of the stimulus to −20 db, the rate of discharge of this unit decreased, giving a new average discharge rate of 256 pulses per second, and the width of the resulting histogram increased, giving a standard deviation of 2.8 msec.

The distribution of intervals fell in an exponential manner from the modal value to the longer intervals. A striking characteristic of these units was that the modal value of their interval distributions was constant for all levels of excitation of the unit, although the mean interval and standard deviation of the distributions changed.

In contrast to these units, one neuron was observed with an approximately bell-shaped distribution of discharge intervals. Histograms for this unit are shown in Fig. 2, measured with a class interval duration of 5 msec. In the spontaneous state the mean discharge rate for this cell was 28 pulses per second, and the standard deviation was 11.9 msec. During stimulation the modal value of discharge shifted to a shorter interval. The mean discharge rate for this state was 178 pulses per second, and the standard deviation was 2.3 msec. This type of behavior is more typically seen in units in the central somatosensory pathways (*4*).

The exponential character of the distribution of intervals of discharge observed in units in the cochlear nucleus suggests that a Poisson type of random process is involved in the generation

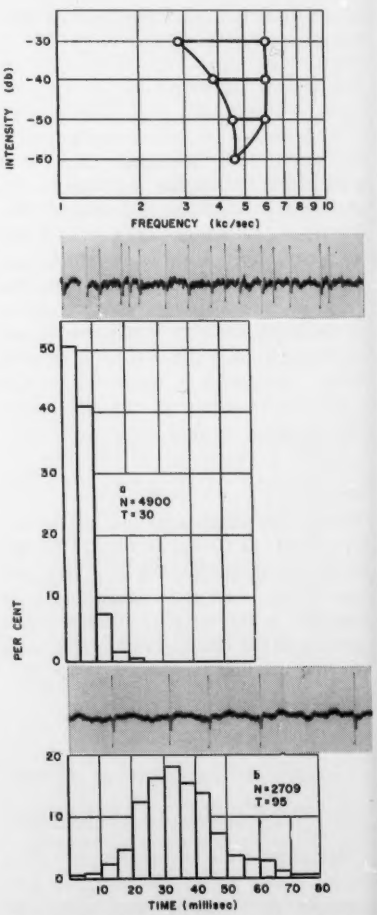

Fig. 2. Cochlear nucleus unit, anesthetized cat. Histograms of discharge intervals: *a*, stimulation of the ipsilateral ear with a tone of 4.5 kcy/sec at a level of −40 db (20 db above threshold); *b*, spontaneous activity.

of trains of impulses in these units. At shorter intervals the recovery processes of the neuron limit the generation of impulses, preventing the distribution from being truly exponential.

The highly irregular character of the discharge patterns observed in response to stimulation with pure tones, and the general similarity of the interval distributions for most units, appears to preclude any simple interpretation of the coding of tone frequencies by the pattern of impulses carried by individual neurons.

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6. We wish to thank R. Galambos for his constant encouragement and advice during the course of the experiments and also G. Moushegian and A. Rupert for their collaboration in the collection of data.
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Search for Evidence of Axial Current Flow in Peripheral Nerves of Salamander

Abstract. The demonstrated association of the d-c bioelectric field with central nervous system elements implies the longitudinal flow of charge carriers within that system. Transverse d-c voltages, attributed to the Hall effect, have been obtained from the extremities of intact salamanders under circumstances suggesting such electric current. These voltages disappeared after nerve section, and their magnitude was related to the depth of anesthesia.

The d-c or steady-state, bioelectric field has been studied extensively (*1*), and has been found to correlate with growth (*2*), tissue repair (*3*), tumor formation (*4*), cephalocaudal relationships (*5*), sleep state in man (*6*), and human behavior (*7*).

Recently, precision determinations have shown that this bioelectric field is a complex one, with multiple sources and sinks bearing a close spatial relationship to the anatomical arrangement of the central nervous system (*8*). This observation led to the theory that the d-c field is generated within and distributed by elements of this system and that it might further represent a primitive data transmission mechanism of neural or neural-related tissue. This theory is at variance with the views which hold that the d-c field is generated by the sum total of electrical activity of all of the cells of the organism and that it possesses no specific organization other than cephalocaudal polarity (*9*). Implicit in the thesis is the necessity for longitudinal movement of electrical current carriers within the neural structures, and demonstration of such a phenomenon would be necessary for further substantiation. The Hall effect (generation of a potential gradient at 90° to the direction of current flow in the presence of a steady-state magnetic field, oriented at 90° to the direction of current flow and also at 90° to the potential gradient) was selected as evidence to be looked for in support of the hypothesis of axial current flow.

Adult salamanders (*Triturus viridescens*) were used since the d-c field has been completely mapped in this animal. Intact extremities were utilized rather than nerve fibers dissected free to prevent interference from currents of injury. The nerves, however, can be completely severed by fairly simple surgical approaches at a distance far enough away from the recording electrodes to avoid pickup of injury currents. Electrodes were silver-silver chloride, saline-filled, with thin, terminal, cotton wicks. The magnetic flux was obtained from a 7000-gauss permanent magnet with a ⅜-in. air gap, mounted on a movable nonmagnetic support. The electrode contacts were placed just proximal to the elbow joint in such fashion that a line joining both contacts would be 90° to the long axis of the limb and oriented in a cephalocaudal direction.

The magnet was so arranged that, when it was swung into position, the flux field completely encompassed the areas of electrode contact, with the field direction oriented 90° to the line joining the electrodes. Movement of the magnet was without mechanical vibration, and care was taken to insure that no portion of the magnet or its support came into direct contact with the animal. Potentials were amplified by a chopper type direct-coupled preamplifier and a d-c power amplifier. All determinations were carried out in a double-walled Faraday cage, and the experimental setup was as shown diagrammatically in Fig. 1.

The electrodes alone making contact through a drop of saline demonstrated a steady potential of 25 μv. No change in this potential was obtained with the application of the magnetic field other than the voltage transients associated with movement of the field in and out of position (Fig. 2*A*). These transients averaged about 4 sec in duration. In the animal experiments, once the magnet was swung into position it was left stationary for from 20 to 60 sec, a time more than sufficient to permit decay of the transients.

In all 24 salamanders tested, transverse d-c voltages of from 10 to 150 μv were obtained during the period of steady-state magnetic field application. Removal of the magnetic field brought about a return to the original base line.

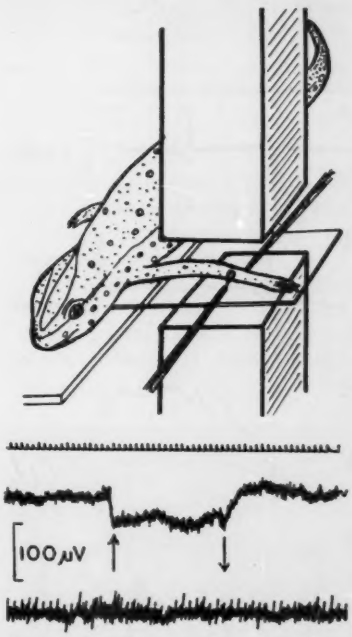

Fig. 1. (Top) Schematic view of the experimental apparatus with the magnet poles swung into place. All portions of the apparatus are made of nonmagnetic materials. The long axis of the limb, the direction of the magnetic flux field, and the inter-electrode line are all at 90° to each other. (Bottom) Top trace is a time marker with 1-sec intervals. The second trace is a typical Hall voltage, the transients of opposite sign indicating magnet movement. The arrow pointing up indicates movement of the magnet into position; pointing down indicates movement out of position. The lower trace is the electrocardiogram measured from precordium to the right extremity—the rate here is about 50 per minute with irregularities.

d-c voltage. The transverse voltages were steady for as long as the magnet remained in place and showed no fluctuation synchronous with blood flow pulsations (Fig. 1). The amplitude of the voltages obtained appeared to be related to the level of anesthesia, being absent during deep anesthesia and increasing in amplitude as recovery occurred. During light anesthesia, two types of slow wave forms appeared in the voltage record. One had a period of approximately 1.25 sec, the other of 15 to 20 sec. These were usually of sufficient magnitude to mask the shifts in the base line unless their magnitude was quite high (Fig. 2*C*). The clearest records were obtained during moderate anesthesia prior to the appearance of the slow wave forms (Fig. 2*B*).

In five of the specimens, the brachial plexus was exposed through an anterior incision on the thorax, and it was found possible to section all of the nerves without interfering with the blood supply to the extremity. (Blood flow in the digital vessels is easily visualized with a magnification of 20 and was not markedly altered by this procedure.) After the nerve section, no transverse voltages could be obtained in response to an applied magnetic field in any stage of anesthesia, and the transverse voltages of the contralateral, nondenervated limb declined markedly. The normal d-c field voltages (longitudinal) in the intact animal average from 10 to 30 mv between the brachial area of the spine and the extremity tip, with the tip negative. After brachial plexus sectioning, these voltages drop to about 10 percent of their normal value, and frequently the voltages on the contralateral limb decrease by 50 percent or more.

Fig. 2. Transverse voltages obtained under the conditions indicated in each case. Arrows indicate magnet movement as in Fig. 1. (*A*) Voltage measured from the electrodes alone with and without magnetic field. No d-c shift is observed (50 μv/cm). (*B*) Example of the usual Hall voltage found in moderate anesthesia (100 μv/cm). (*C*) Example of high magnitude Hall voltage noted during recovery phase of anesthesia; the two types of slow waves are clearly visible (100 μv/cm). (*D*) Transverse voltage measurements after nerve section; no evident Hall effect is visible (50 μv/cm). (*E*) Voltage after section of cord at medulla (50 μv/cm).

In the intact animal, sectioning of the spinal cord at the level of the lower medulla results in a marked drop in the d-c field voltages in both forelimbs to about 10 percent of their normal value. In this case the transverse voltages also promptly disappeared in the same extremities along with the slow wave pattern.

Since a stationary magnetic field can have an effect only on charge carriers moving at right angles to the field, then the transverse voltages obtained are interpreted as Hall voltages, resulting from longitudinal charge carrier movement in the extremity. The independence of the observed voltages from the pulse rate, and the disappearance of these voltages after nerve section alone, indicate that the charge carrier flow is related to the peripheral nerves and that blood flow is not the parameter being measured. That the observed effect is dependent upon the functional state of the nervous system is further evidenced by the amplitude changes with different levels of anesthesia and by the change in the transverse voltages in the contralateral limb after nerve section on the opposite side. The action potential spike is presumably associated with ion movements in a direction transverse to the long axis of the axon. This direction of movement, the low mobility of ions, plus the steady state of the observed transverse voltages mediate against this activity being a factor in the production of the phenomenon.

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8 May 1961

Variable Expressivity of a Mutant Gene in Leopard Frog

Abstract. The genetic distinction between the nonspotted, or burnsi, mutant and the common-spotted, wild-type leopard frog is not simply unifactorial. The burnsi phenotype is a manifestation of genic interaction between a major pigmentary locus and a complex of modifiers (minor genes with small effects).

The disciplines of genetics and embryology converge in the search for the causality of development and differentiation. Regrettably, the paucity of genetical data in amphibians contrasts sharply with the wealth of embryological knowledge of the group. Whatever genetical information has accumulated has been admirably used to study the role of genes in development. Witness, for example, the biochemical analysis by Baker (*1*) of the nonspotted (burnsi) mutant of the common leopard frog (*Rana pipiens*) and the nuclear transplantation experiments by McKinnell (*2*) involving the mottled (kandiyohi) deviant of the common leopard frog. Each of these variant pigmentary traits is seemingly based upon a simple mode of inheritance (*3*, *4*). However, it should be recognized that more intensive analyses would undoubtedly reveal complexities in the mode of transmission of the traits, which, in turn, would complicate embryological findings dependent upon the genetical data. This is attested by the results of a protracted investigation on the inheritance of the nonspotted (burnsi) pattern, which was heretofore thought to differ from the wild-type pattern by a single dominant gene.

J. A. Moore (*3*) demonstrated that the burnsi gene (designated *B*) exerts a dominance over the wild-type or

common-spotted allele (*b*). A major mutant gene is involved, but present investigations (*5*) reveal that modifiers (spotting genes with small effects) alter the magnitude of expression or dominance of the major burnsi gene. The action of modifiers is recognizable in the phenotypes of heterozygous burnsi frogs (*Bb*). Heterozygous burnsi frogs range from those devoid of dorsal spots (type "A" in Fig. 1) to those containing spots on the arms and legs, varying in size, shape, and number (types "B" to "E"). The spotting of the appendages of type "E" approaches the condition found in the wild-type leopard frog. Type "F" is a unique burnsi frog, possessing a large number of spots on the appendages as well as a patchwork of melanophores on the back (*6*).

The modifiers or minor-spotting genes (designated "+") are integral parts of the genetic system of the wild-type frog. The modifying genes most likely were established in the distant past in the wild-type stock to protect or "buffer" the main pigmentary locus against variations, both genetical and environmental. The modifiers have slight effects, virtually undetectable, in the normal genotype (*bb*). These modifying genes, however, have observable effects when the wild-type main gene is altered. The burnsi mutation (*B*) represents an alteration of the main pigmentary locus. The burnsi mutation tends to reduce pigmentation markedly, but the activity of this mutant gene is mitigated by spotting modifiers.

It has not been possible to ascertain the exact number of modifiers nor to dissociate the complex into single-gene components. This, however, does not invalidate the contention that modifiers are operative. One of several experiments is presented below that not only reveals vividly the presence of modifiers but also focuses attention on unsolved and new problems.

In the experiment, a burnsi male with heavily-spotted appendages (type "E" in Fig. 1) was crossed with a wild-type leopard frog. The cross yielded 32 common-spotted (wild-type) and 37 burnsi offspring, or 1:1 ($p > .50$). The burnsi male was thus heterozygous at the main locus (*Bb*). The spotting patterns of the burnsi progeny were variable, reflecting the segregation of spotting modifiers. Two of the 37 burnsi offspring were of type "C", 8 of type "D", and 19 of type "E". No offspring specifically resembling type "F" was recovered; however, in the remaining eight burnsi offspring, the melanophores tended to aggregate or had actually aggregated into one, two, or three discrete spots on the dorsum. Apparently, these dorsum-spotted heterozygous burnsi offspring (Fig. 2, top row) tend in the direction of the common-spotted (wild-type) frogs because of the presence of numerous spotting modifiers.

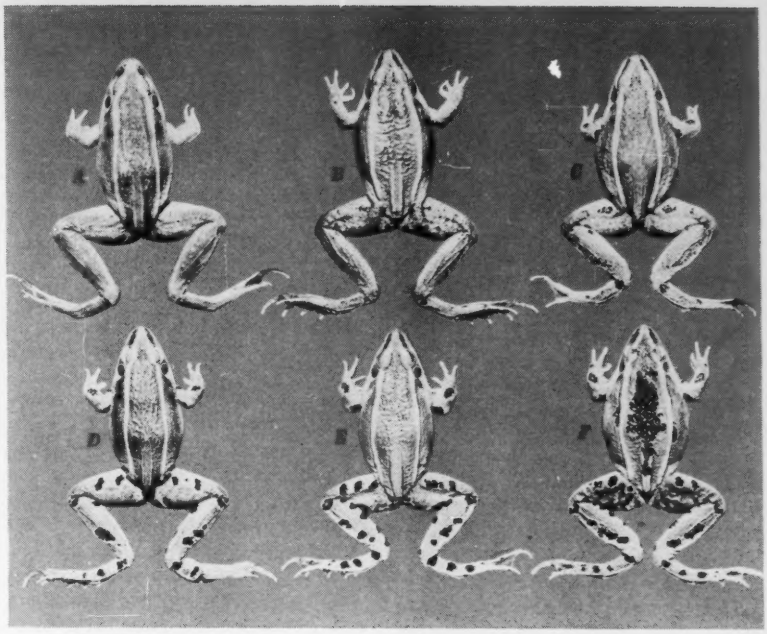

Fig. 1. Degree of variability in the expression of the burnsi character, reflecting the activity of modifiers (minor-spotting genes). No or few spotting modifiers are present in type "A"; increasing numbers of modifiers occur in types "B" to "F".

It should be noted also that there is considerable variation in the extent of dorsal spotting (that is, between the dorsolateral folds) in wild-type indi-

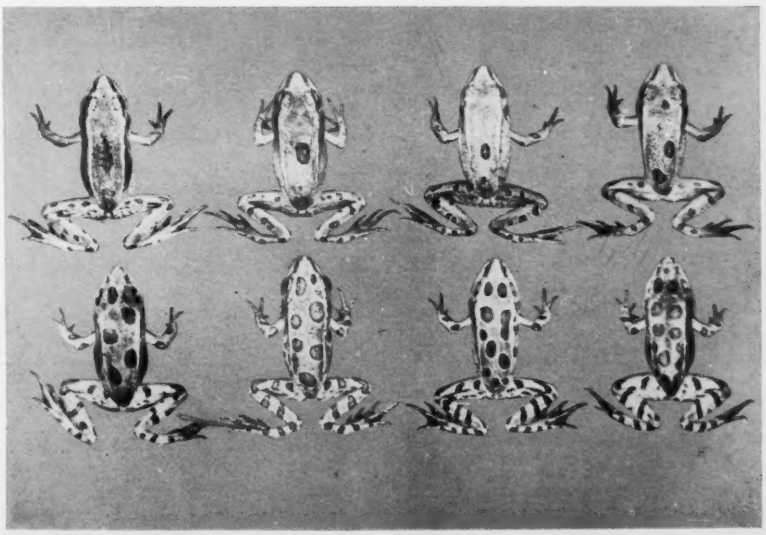

Fig. 2. Dorsally spotted heterozygous burnsi offspring (top row) and common-spotted, wild-type offspring (bottom row) derived from a cross of a type "E" burnsi frog (illustrated in Fig. 1) with a common-spotted, wild-type frog.

viduals (Fig. 2, bottom row). The number of dorsal spots among the progeny classified as wild-type ranged from 5 to 14. The gap between a burnsi and a wild-type individual is almost closed, leading to the perplexing query: How many dorsal spots must an individual contain before it is classified as a burnsi or a wild-type?

The situation is further complicated by the finding that the frequency of burnsi frogs may be as high as 10 percent in populations of leopard frogs in Minnesota (*7*). This supposedly rare mutant occurs too frequently in natural populations to be maintained solely by mutation pressure. The burnsi gene is probably being fostered by some selective advantage conferred upon the heterozygote. It is tempting to suggest that selection is promoting the accumulation of minor *nonspotting* genes ("–" modifiers) that enhance the activity of the burnsi gene (or counteract the effects of the "+" modifiers). Thus, it may be that there are two optimal phenotypes—the completely unspotted heterozygous burnsi frog (type "A") and the wild-type frog. The intermediate burnsi phenotypes (types "B" to "F") may be less advantageous or disadvantageous, and a sharp dimorphism may ultimately result. In essence, the burnsi gene, presently behaving as a semidominant, may eventually become completely dominant as a result of persistent selection for nonspotting modifiers.

The investigations thus far have raised more questions than have been answered, but it is apparent that an extended analysis is required to unravel the intricacies of a seemingly simple anuran trait.

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13 March 1961

Variations in Thermal Sensitivity

Abstract. In the past, confusion has resulted from the use of relative expressions indicative of the direction of temperature change, rather than positive identification of warm and cool sensations. Data are presented which show that at more extreme skin temperatures sudden changes in temperature may result in two readily discernible sensations. The occurrence of each sensation depends upon the magnitude of the change.

Investigations of thermal sensitivity (*1*), which have related changes in the thermal threshold to skin temperature, have been concerned with the quantitative aspects of the thermal sensation—for example, the occurrence of a detectable change in sensation accompanying a rapid change in skin temperature. The qualitative aspects of sensation—for example, whether the sensation is warm or cool—have not been investigated. It has been assumed that when the skin temperature is raised, warmth will be experienced, whereas reducing the skin temperature will result in a cool sensation. While this is generally true, it is not always the case, as may be seen in the data presented here (*2*).

The stimulator was constructed of a hollow Lucite block 25 by 35 by 25 mm. The top was open and the bottom was a 20- by 30-mm silver plate, 0.025 mm thick. Water from constant-temperature baths was directed into the stimulator through either of two jets. Switching from one jet to the other produced a change in the temperature of the silver plate with a time constant of 0.4 sec. A thermistor inside the chamber, in contact with the middle of the silver plate, monitored the temperature of the water. Temperature changes of as little as 0.025°C could be produced with ease.

The subject was seated in an adjustable chair with the stimulator placed on the dorsal surface of the forearm 1 in. from the bend of the elbow. Water was circulated through the stimulator at the adapting temperature. After a minimum of 20 min, which allowed the subject to adapt to the room temperature and the skin beneath the stimulator to reach a reasonably stable temperature, threshold measurements were be-

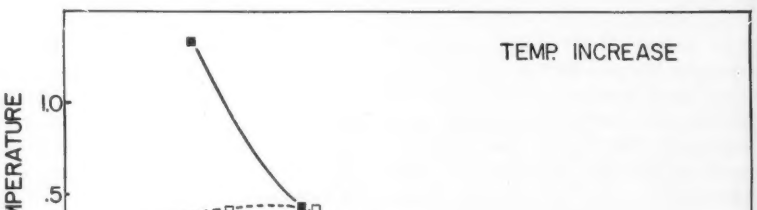

Fig. 1. Changes in the absolute threshold (solid squares, solid curves) and in the just noticeable difference threshold (open squares, broken curves) resulting from the temperature to which the skin was adapted. Male and female subjects showed the same thresholds to both increments and decrements in the adapting temperature except as shown by curve 1 (males) and 2 (females). The vertical dimension of the squares used to plot the mean thresholds represents about 0.07°C on the ordinate. The standard error of each mean threshold did not exceed the size of the square, except on curve 1 at an adapting temperature of 42°C, where it was 0.103°C.

gun. These followed the psychophysical method of limits. The threshold was the mean of ten ascending and ten descending series for each subject. These were obtained in two sessions, one in the morning and the other in the afternoon.

Two criteria of "threshold" were used. In one, the subjects were required to report when they could perceive a change in the thermal sensation produced by a change in the stimulator temperature. These thresholds appear in Fig. 1 as open squares and are henceforth referred to as the "just noticeable difference" (jnd) thresholds. The other criterion required the subjects to identify the sensation as being either warm or cool. These thresholds are shown by filled squares in Fig. 1 and are referred to as absolute thresholds.

Two males, ages 21 and 38, and two females, ages 20 and 26, were the subjects in these measurements. None of the subjects had any known physical defects which might impair their sensitivity to temperature changes. Each subject had received more than 30 hr of practice in making the discriminations prior to threshold measurements. The thresholds of the subjects were averaged, except the thresholds to temperature reductions at adapting temperatures above 33°C. Here the males (curve 1) and females (curve 2) differed so markedly that they were plotted separately.

Figure 1 shows that the just noticeable difference curves follow those of the absolute thresholds throughout most of the range of adapting temperatures. However, the thresholds to temperature increments diverge at low adapting temperatures, while those obtained from temperature decrements diverge at high adapting temperatures. This suggests a change in the conditions of measurement, which appears to be related to the degree of sensory adaptation experienced by the subjects at the various adapting temperatures. All the subjects failed to adapt completely (complete loss of thermal sensation) to temperatures below 33°C. Additional time did not change the level of adaptation. The subjects invariably reported a persisting cool sensation. Increments in the stimulator temperature of 0.4°C could be detected as a change (just noticeable difference threshold). Considerably greater changes had to be produced for the subjects to identify the change as "warm." Increments in the stimulator temperature of greater than 0.4°C, but less than that required to produce a sensation of warm, were identified as "less cool."

When the subjects were adapted to temperatures greater than 33°C, increments in the stimulator temperature were readily detected and no differences were observed between the just noticeable difference and the absolute thresholds.

The female subjects reported complete sensory adaptation to higher temperatures (41°C) than males did (36°C). The thresholds obtained by decrements in the stimulator temperature started to diverge at these points. At higher adapting temperatures a persisting warm sensation was experienced throughout the threshold measurements. While decrements in temperature of as little as 0.6°C could be detected, they did not result in a cool sensation; much greater changes were required. Changes of more than 0.6°C, but less than that required to produce a cool sensation, resulted in reports of "less warm."

In general, these data show that small rapid changes in skin temperature produce sensations appropriate to the direction of the temperature change. However, when the skin temperature is low, small increments can be detected, but result in sensations of less cool. Larger elevations are required to produce a sensation of warm. When skin temperature is high, sudden small reductions can also be perceived but are sensed as less warm. Larger changes are required before cool is experienced.

The elevations of the absolute warm threshold at low adapting temperatures and the absolute cool threshold at high adapting temperatures are indicative of the manner of operation of the thermal receptors. Two explanations appear possible at this time. First, the variations in thermal thresholds observed here may have resulted from changes in the thermodynamics of the tissue due, perhaps, to the greatly altered cutaneous blood flow in response to the temperature to which the skin is adapted. If tissue thermodynamics were the only consideration, one would expect that the just noticeable difference threshold, as well as the absolute threshold, would be altered equally. It is obvious that this is not the case. It might also be expected that both the warm and cool absolute thresholds would be affected at both extremes of the adapting temperature. A second explanation must be entertained—that of altered receptor sensitivity resulting from the temperature at which they are required to operate. Kenshalo and Nafe (*3*) have reviewed a theory of thermal reception, presented earlier by Nafe (*4*), which is based on the direct action of thermal energy upon the smooth muscle of the cutaneous vascular system. It predicts changes in thermal sensitivity associated with changes in the skin temperature.

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23 March 1961

Dating Desert Ground Water

Abstract. Tritium in Arabian rainfall has followed the trend observed in North America with peaks in 1958 and the spring of 1959. These measurements will be useful for future hydrologic studies. Water from wadi gravels averages 10 yr old. Carbon-14 measurements of deep waters indicate ages of several thousand years.

Samples of water collected by the Arabian American Oil Company in the course of field operations in Saudi Arabia during the past 2 yr were made available for analysis in the tritium and carbon-14 laboratories of the U.S. Geological Survey to help evaluate the use of the radioactive isotopes in studies of desert ground water.

Some of the samples of deeper ground water tested for tritium indicated an age (time since exposure to atmospheric supply) older than the limiting time span of about 50 yr measurable by this technique. However, values of 3.7, 3.8, and 5.2 tritium units (T atoms per 10^{18} H atoms) with a possible error of $\pm$ 0.5 came from three samples from "wadi" gravels in the central region of the Arabian peninsula, from which the age of waters in the lower part of a great incised dendritic drainage system seems to be on the order of 10 yr (as of 1958), unless fallout from 1952–54 hydrogen bomb explosions had spread into the system. The location of the wells, the

Table 1. Precipitation data.

Sample No.	Date	Tritium units* (av. error, ± 8 percent)
	Dhahran	
352	5–6 March 1959	112
	Near Dhahran	
353	7–8 March 1959	96
354	7–8 March 1959	124
	Rub' al Khali area, showers	
420	25 May 1959	63
423	25 May 1959	69
421	26 May 1959	59
422	26 May 1959	54
	Rub' al Khali area	
604	1 January 1960	20
606	3 November 1960	18

* Tritium atoms per 10^{18} hydrogen atoms.

presence of calcium carbonate cement in the upper part of the gravel fill in downstream gorges, and the distances up-wadi to where slopes of stream beds are above grade lead us to believe that there was no man-made tritium in these waters. On the other hand, water from a large open dug well in Wadi Aleysan at Riyadh tested 8.9 tritium units, evidently indicating a mixture of more recent tritium-enriched water with older water seeping out of the gravels in the walls of the well. A year later, rain samples from the Persian Gulf and Rub' al Khali regions gave values up to 124 tritium units, which correspond to the Northern Hemisphere spring tritium peak observed elsewhere. Later rains show the tritium-level decay characteristic of later 1959 and 1960. Tritium values for precipitation are given in Table 1. The value of the large increase in tritium from bomb fallout in infrequent desert rainstorms remains to be evaluated, but certainly age determinations of water in the shallow gravels of the desert will have to be checked by other methods during the next several years.

The C^{14} determinations give hope of widespread use for dating older and deeper desert waters. Six samples consisting of the bicarbonate and CO_2 extracted from deep water samples (Table 2) were analyzed for C^{14} content to determine the time since their precipitation as rainfall. The waters came from aquifers more than 1200 ft below the land surface at the wells. The distances from the outcrop of the aquifers to the wells range from 24 to 250 km.

The method of dating ground waters by their C^{14} content has been applied in the German till plains by Brinkman *et al.* (*1*). The age computations made by Brinkman and his co-workers of the water in this humid carbonate-rich area are based on an initial C^{14} content of 85 percent of modern wood. This subtracts approximately 2000 yr from their dates. In the low-latitude deserts, it is believed that the rainfall, episodic and often violent in nature, adds water directly to the nubian-type sandstones and dunes above the sandstones without uptake of "dead" carbonate. For this reason, the ages of these samples were computed on the basis that the initial C^{14} was the same as that of contemporary wood, or more exactly, 95 percent of the National Bureau of Standards oxalic acid C^{14} standard. The uptake of "dead" carbon by the solution of limestone during transport of the water through the aquifer would tend to be inhibited by the increased temperature (decreased CO_2 solubility) as measured by the geothermal gradient. The ages for the deep artesian waters at Buraida, Riyadh, Khurais, and Abqaiq range from 20,400 to 24,760 yr. This time span is of the same order of magnitude as an estimate of 18,500 yr for the water to move from the outcrop to Abqaiq, as calculated by Whitman Dimock of the Arabian American Oil Company from pumping test data and broad assumptions of aquifer coefficients (*2*). The climax of the Wisconsin glacial stage occurred at about this time, and the high rainfall during this pluvial period must have charged the aquifers. The ages greater than 33,000 yr for the water samples from the western Rub' al Khali may be due to old carbonate taken up from the carbonate rocks in the Yemen highlands and the calcareous loess east of the highlands, or they may be the true age of the water there, which would have fallen as rain during the early Wisconsin glacial stage (*3*).

Table 2. Carbon-14 ages in deep waters of Saudi Arabia. WW, water well.

Sample No.	Water well	Depth of sample (ft)	Age of aquifer	Min. distance to outcrop (km)	Water	
					Temp. (°F)	Age (yr)
W-904	Town well, Buraida	1250	Cambrian and Ordovician	24	100	20,400 ± 500
W-889	Riyadh, WW 180	3647 to 3974	Triassic or Jurassic	60	126	24,630 ± 500
W-897	Khurais, WW 8	1490 to 1693	Cretaceous	70	80	20,760 ± 500
W-894	Abqaiq, WW 32	3003 to 3402	Cretaceous	250	134	22,500 ± 500
W-888	St. WW 7	1617 to 3035	Jurassic and Cretaceous	75	100	> 33,000
W-887	St. WW 13	3435 to 3506	Permian	200	98	> 33,000

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17 February 1961

Haptoglobin and Transferrin Gene Frequencies in a Navajo Population: A New Transferrin Variant

Abstract. The distribution of serum haptoglobin, transferrin, and ceruloplasmin has been studied by starch gel electrophoresis for a Navajo Indian population in Arizona. Only the three common haptoglobin phenotypes were observed, but a high percentage of a new faster-moving transferrin variant B_{0-1} was discovered. No unusual ceruloplasmins were found.

The development of starch gel electrophoresis and the subsequent discovery of the genetic basis of human serum haptoglobin types (*1*) have led to an unprecedented proliferation of gene frequency estimates for the two common haptoglobin alleles in numerous population groups. In the comparatively short period of 5 yr, the world haptoglobin map has been rapidly filled. As tabulated by Sutton *et al.* (*2*), the Hp^1 frequency ranges from a low of .09 for Malaya Indians to a high of .87 for Nigerian Negroes and of .93 for Lacandon Indians in Central America. An interesting feature of the haptoglobin map is the progressive increase in Hp^1 frequency from Southeast Asia via Alaska and North America to Central and South America.

A genetic basis has also been established for the inheritance of human

transferrins (*3*), the β_1 iron-binding globulins in serum. Nine different molecular species of transferrin have been distinguished by their starch gel mobilities. In addition to the eight types previously reviewed (*4*), an additional variant D_4, of intermediate mobility between D_0 and D_1, has recently been described by Harris *et al.* (*5*). However, the high frequency of the common transferrin C allele has made population studies more difficult than for the haptoglobins, and only rare examples of homozygotes for the unusual alleles have been reported.

In the present study, haptoglobin and transferrin types were determined for a large group of Navajo Indians in Arizona. Starch gel electrophoresis was carried out in borate buffer at *p*H 8.6 in the vertical system described by Smithies (*6*). A compact apparatus has been designed which permits simultaneous vertical electrophoresis of 96 separate sera in six trays of 16 slots each. Hemoglobin and radioactive iron were added to the samples, and after electrophoresis each gel was sliced into three layers. The top slice was stained for protein with amido black, and the bottom slice was treated with benzidine reagent (0.2 g of benzidine in 100 ml of 50 percent ethanol, 0.2 ml of H_2O_2, and 0.5 ml of acetic acid) for detection of haptoglobin type. Transferrins were identified by autoradiography (*7*), and individual patterns were classified by their mobilities relative to known standard types. The use of autoradiography was of considerable value in the determination of transferrin types. Although transferrin C was readily detected by its characteristic shape and position in the protein stain, the faster moving B types were sometimes obscured by ceruloplasmin and the slower moving D types by haptoglobin. Autoradiographs were made from the middle slice of the gel in order to avoid the slightly blurred patterns caused by trailing at the surfaces of the gel during electrophoresis. The middle slice was subsequently stained for ceruloplasmin with *p*-phenylenediamine (*8*).

Haptoglobin and transferrin types for the Navajo population are given in Tables 1 and 2. No differences in ceruloplasmin mobility were observed in 263 indivduals analyzed. The 0.454 Hp^1 frequency in the Navajo population is significantly different ($P < 0.001$) from the only previously reported data on American Indians, a frequency of 0.59 determined for 98 Apaches (*9*). However, the authors of the Apache survey suggested that their Hp^1 frequency may have been overestimated because of difficulties in differentiating free hemoglobin from the haptoglobin 1–1 band in the horizontal gel system which they used. In the present study the vertical gel system provided clear separation of these two components. Every sample could be placed in one of the three common haptoglobin classes. No sample was observed with the rare phenotype Hp^{2-1} (mod) and no *Hp* 0 types were found. As indicated by the value for P of $> .10$, the distribution of observed phenotypes was in reasonable agreement with that expected under Hardy-Weinberg equilibrium.

Table 1. Haptoglobin types in Navajo Indians. The method of estimation of gene frequency is shown below the table.

No. in family* (n)	Total individuals	1–1 (a)	2–1 (b)	2–2 (c)	$2a + b$ (x)	$2(a + b + c)$ (y)	Weight per gene $[w = 2/(n + 1)]$
Unrelated	169	39	80	50	158	338	1.0000
2	54	10	25	19	45	108	.6667
3	21	6	8	7	20	42	.5000
4	4	1	3	0	5	8	.4000
5	15	1	3	11	5	30	.3333
Total	263	57	119	87	233	526	

* Family consists of either parent and children or children alone.

$\Sigma wx = 201.7$ $\Sigma wy = 444.2$ $p^{Hp^1} = \Sigma wx/\Sigma wy = .454$ Std. error S.E. $= (pq/\Sigma wy)^{1/2} = .024$

$\chi^2 = 2.084$ $P > .10$

In addition to the Navajo data, preliminary studies have also been carried out on an Araucanian Indian population near Temuco, Chile (*10*). An Hp^1 frequency of .75 was obtained for 34 individuals, which is in agreement with a value of .73 determined for 173 Peruvian Indians (*11*).

It is difficult in many cases to make accurate comparisons of haptoglobin frequencies in various populations because reports have seldom included the standard error of the observed gene frequency. The standard error is defined as

$$\sigma = (pq/T)^{\frac{1}{2}}$$

where p and q are observed frequencies for the two alleles and T represents the number of *independent* genes analyzed. If gene frequency data from small populations are to be compared, it is necessary that an accurate value of T be obtained in order that a reliable standard error may be calculated. For unrelated individuals, T will equal twice the number of individuals, but where the sample includes related individuals, the value of T must be reduced. Cotterman (*12*) has described a highly efficient system of weighting for determining the number of independent genes in a related sample, and this method has been applied to the Navajo population. Where both parents in a family have been included, all four genes in the family are accounted for, and no further information is gained from the offspring. Where the family consists either of parent and children or of children alone, Cotterman assigns a weight w for the genes in the family which varies with the size of the family and which is calculated as $w = 2/(n + 1)$, where n equals the number of individuals in the family. As the family size increases, the number of independent genes in the family approaches four. The detailed calculation of the haptoglobin gene frequency and the standard error is given in Table 1. A similar calculation was made in the case of transferrin.

Of the 17 unusual transferrin variants found in the population, 16 were of a previously undescribed molecular species of intermediate mobility between transferrins B_0 and B_1 (*13*). In the established transferrin nomenclature, variants which are faster-moving than C are labeled B and slower-moving variants are labeled D, and subscripts in order of decreasing mobility are used to distinguish transferrins within the two classes. According to this system, it is suggested that the new Navajo transferrin be designated B_{0-1}. In addition, one Navajo individual was of transferrin type B_2C, which has an inci-

Table 2. Transferrin types in Navajo Indians.

Total individuals	Total independent genes	CC	$B_{0-1}C$	B_2C	$p^{B_{0-1}}$	S.E.	χ^2	P
230	393.27	213	16	1	.041	.010	.625	$>.40$

dence of approximately 1 percent in English (*13*) and Canadian (*14*) whites. The 8 percent incidence of phenotype $B_{0-1}C$ is the highest value yet reported for any of the faster-moving transferrin B types, although its incidence is somewhat lower than the average value of 10 percent for type CD_1 in Negro populations and the high of 15.6 percent CD_1 reported for a large population in the New Guinea highlands (*15*).

No factors are known which could maintain the transferrin polymorphism (*16*), although some of the variants may be important for resistance to infectious disease. In this connection it may be possible to relate the wide prevalence of tuberculosis and streptococcal infections in Navajo populations (*17*) to the work of Martin and Jandl on the inhibition by transferrin of viral multiplication and cytopathogenic effects (*18*). If the frequencies of the unusual genes are stable, the similar incidence of $B_{0-1}C$ in Navajos and of CD_1 in Negroes suggests that selective factors of approximately equivalent intensity may be operating in the two populations. The development of a method for the separation and isolation of rare transferrins from the serum of heterozygotes (*19*) has permitted experiments to be undertaken to investigate the nature of the chemical differences among the various transferrin types (*20*).

Note added in proof. Since the submission of this report, we have identified in a Chinese population a transferrin variant of slightly greater electrophoretic mobility than the Negro D_1. The conditions required to demonstrate this difference suggest that the Chinese variant will prove slower-moving than the D_1 of Harris *et al.* (*5*).

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Intrinsic Barriers to Dispersal in Checkerspot Butterfly

Abstract. Capture-recapture studies revealed that the checkerspot butterfly *Euphydryas editha* is extraordinarily sedentary. Since no physical barriers prevent interchange between various portions of the study colony, it is concluded that intrinsic factors play the major role in limiting movement. The few available data on dispersal are discussed.

It is generally accepted (*1*) that most flying organisms display a high degree of vagility, the ability to cross barriers. Nevertheless, as Mayr (*2*) has pointed out, birds are usually quite sedentary and make little use of their dispersal potential. Similarly, the few butterflies which have been studied with any degree of rigor—*Maniola jurtina* L. (*3*), *Polyommatus icarus* Rott. (*4*), *Papilio glaucus* L. (*5*), *Anthocaris sara* Boisduval (*6*), and *Pieris protodice* Boisduval and Leconte (*7*)—have shown a remarkable lack of wanderlust. The present report on *Euphydryas editha* Boisduval (Nymphalidae: Nymphalinae) further underscores the importance of differentiating *potential* and *actual* vagility and emphasizes the dangers of casual assumptions about dispersal patterns, "gene flow," and the like.

In the San Francisco Bay region, *Euphydryas editha* is confined to areas of serpentine outcropping, where its food plant, *Plantago erecta* Morris, is especially abundant. In the spring of 1960 a capture-recapture study was made of the adult population of this butterfly on Stanford University's Jasper Ridge Biological Experimental Area, as part of a long-term investigation of microevolution in this species. There *E. editha* is found only in a hilltop island of grassland, surrounded by dense chaparral and scattered oak woodlands. During the 25-day flight period (31 March to 24 April) 185 individuals were given distinguishing marks and released (*8*). Of these individuals 97 were recaptured at least once, accounting for a total of 224 recaptures. The population size (total number of individuals involved in the flight) was estimated to be between 250 and 400. Sampling was done once a day, so that all recaptures of any given individual were on different days.

Prior to the flight period the region occupied by the colony was arbitrarily divided into eight areas (A to H), and during the flight period a careful record was made of the areas in which the individuals were captured and recaptured. Centers of abundance were found in three areas (C, G, H). Only 12 captures and recaptures were made in areas peripheral to C (A, B, D, E, F), and for analysis areas A to F were lumped as area C. The distribution of individuals taken is shown on the map (Fig. 1). Each dot represents the *first* capture of an individual; placement of the dots within each of the eight areas is approximate. This pattern of distribution, although representing only part of the data, agrees with the impressions of the total distributional picture formed in the field by the investigator and his assistant.

Of the 97 individuals which were marked and subsequently recaptured at least once, only eight were found to have changed areas during the study, and each of these changed areas only once. Therefore 216 of the 224 (96.4 percent) recaptures were in the area of previous capture.

For reasons which will be dealt with in a future paper, the frequency of recaptures varied from area to area. Scoring only those individuals which were recaptured at least once, and ignoring the eight which changed areas, the mean number of recaptures ± standard error (N) per individual were: area C, 1.79 ± 0.210 (34); area G, 2.96 ± 0.523 (24); and area H, 2.52 ± 0.350 (31). The five individuals with the highest number of recaptures in each area had the following scores: area C,

6, 5, 4, 3, 3; area G, 10, 8, 7, 6, 5; and area H, 9, 7, 5, 5, 4. However, if one looks not at the number of times an individual was recaptured but at the number of days it spent "in residence," a different picture emerges. Assuming that no individuals changed areas and then changed back without being detected (a reasonably safe assumption, as this was never observed), one can record the number of days elapsed between initial release and final recapture as the observed number of days in residence. Considering only the individuals recaptured at least once, and again ignoring the eight which changed areas, the average male in area C was known to have been in residence 5.81 days, in area G, 6.33 days, and in area H, 5.61 days. The equivalent figures for females were C, 4.43 days, G, 3.38 days, and H, 3.38 days. An analysis of variance showed a significant effect of sex ($F = 5.78$, $P < .025$) and no sign whatever of an area effect ($F = .19$) or of a sex-area interaction ($F = .12$).

Close scrutiny of the records of the eight individuals that switched areas revealed little of importance. Four were males and four females. Four individuals moved northwest along the main axis of the colony, four moved southeast. Five had wing lengths above the mean for their sex, and three below (no significant difference). Six showed a deterioration in condition between their last capture in their original area and their first recapture in the new area. Two were scored as "fresh" both before and after moving. It would be interesting to know what proportion of dispersing individuals have completed most or all of their reproductive activities before leaving their original area.

It is evident that on Jasper Ridge in 1960 most individuals of *Euphydryas editha*, as long as they remained within the colony, restricted their activities to a very limited area. This lack of movement is shown by the repeated recapture of many individuals in the same location (nearly all of the 71 area G recaptures were made within a space 100 ft in diameter), and by the extreme infrequency of recaptures in areas other than that of original release. No insurmountable physical barriers separate the various sections of the colony. The butterflies were observed on several occasions to fly over the chaparral when chased. As can be seen from the map, in no place does a continuous growth of chaparral or woodland totally separate sections of the colony. In addition, the locations of the main concentrations of individuals remained static, although in areas C and H open space in which the food plant was common was available immediately adjacent to the concentrations. Cursory study of the vegetation and exposure of the areas has not produced a satisfactory explanation of this phenomenon, and further investigations are being made. While it is not known what factors control the spatial distribution of the individuals, it seems that the butterflies "choose" to remain within a circumscribed area—in other words the barriers to dispersal are *intrinsic*.

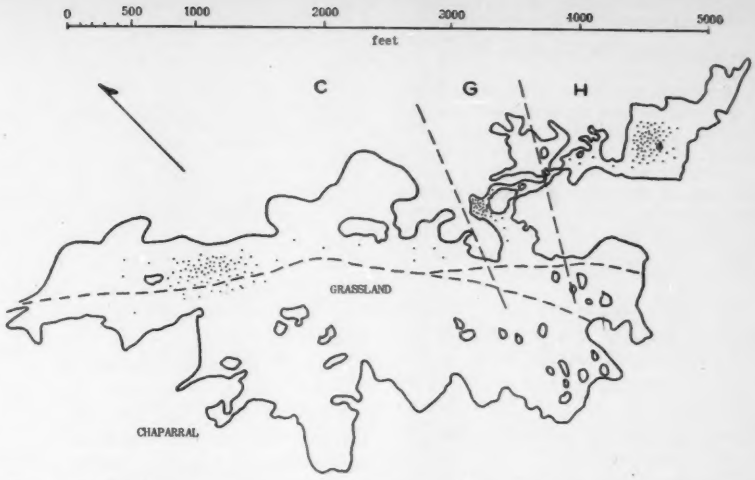

Fig. 1. Distribution of *Euphydryas editha* in Jasper Ridge area, 1960. Each dot represents a single capture. Recaptures are not shown.

Perhaps the most intriguing question raised by the investigation is that of the fate of the 88 individuals which were marked and released but never recaptured. It seems unlikely that the handling procedure affected them (a great many individuals went through the routine repeatedly without any detectable damage). An examination was made of the distribution of recapture frequencies of the first 96 specimens released; these were selected because there was an opportunity to recapture them on a minimum of eight subsequent field days. This showed a disproportionately large 0 class, due to excesses in areas C and H (only 2 of 20 individuals of this group released in G were not recaptured). This difference between the subareas might suggest that individuals are likely to be blown out of the larger, more exposed areas, and thus be lost. However, the general lack of interarea exchange and observations of the butterfly's behavior militate against the idea that the wind would have such a major effect. It is also difficult to hypothesize a mortality factor which could produce this distribution of recaptures. Perhaps there is a heterogeneity of dispersal behavior among individuals within the areas, and differences in the proportions of sedentary and dispersal-prone individuals among areas. Such heterogeneity has been suggested by dispersal data gathered for various groups of Diptera (*9*), and this type of polymorphism could have a distinct selective advantage in a species such as *E. editha* which occurs in rather limited, scattered colonies (*10*).

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Potential versus Time Asymmetries in Adsorption Membranes

Abstract. An outer membrane surface is assumed to take up potassium ions in a manner analogous to adsorption. This model, already successful in predicting transmembrane flux, is shown to predict also an asymmetrical potential-time relation depending on the direction of the concentration changes. The results may have some value in explaining recent observations of similar effects in muscle.

Hodgkin and Horowicz (*1*) have recently reported that asymmetries occur in the time relations when muscle cells are depolarized and subsequently repolarized by altering the external potassium ion concentration approximately instantaneously. The findings are of special interest because, though basically at variance with the classical membrane model employed by Hodgkin and Horowicz, the observed results are predicted and demanded by an "adsorption membrane" model applied to muscle cells by Harris and Sjodin (*2*) and by Sjodin (*3*).

If the method of Sjodin (*3*) is followed in obtaining an expression for the transmembrane flux through an "adsorption membrane," an outer membrane surface is considered to possess N total adsorption sites. Of the N total sites, n sites are assumed to be occupied by potassium ions in any given equilibrium situation. In a nonequilibrium situation, $n(t)$ sites are assumed to be occupied by potassium ions. Only potassium ions in equilibrium with ions adsorbed to sites n are considered to be effective in controlling the membrane potential. Let the external potassium ion concentration be denoted by C_o. When C_o is instantaneously altered to some new value C'_o, the number of occupied-potassium sites n in equilibrium with the concentration C_o changes to some new value, $n + \Delta n$, in equilibrium with the new concentration C'_o. The variable, n, is assumed to change exponentially with rate constants to be derived. Let the two membrane states be denoted by 1 and 2, and the membrane potential by V. The quantities characteristic of each membrane state are then written diagrammatically:

1		2
	From 1 to 2:	
C_o	$n(t)=n_1+(1-e^{-k't})\Delta n$	C'_o
$n=n_1$	From 2 to 1:	$n=n_1+\Delta n$
V_1	$n(t)=n_2+\Delta n e^{-k't}$	V_2

As in the formulation of Sjodin (*3*), the potassium flux onto the sites is j and that from the sites back into solution is j'. The model supposes that "on-flux" is a bimolecular process and is proportional to the external concentration and to the number of available unoccupied sites. "Off flux" is assumed to be a monomolecular process and to be proportional only to the number of occupied sites. Therefore,

$$j = aC(N - n) \tag{1}$$

and

$$j' = bn \tag{2}$$

where a and b are constants of proportionality.

The "net surface flux" is then given by $\bar{j}$ where $\bar{j} = j - j'$ so that

$$\bar{j} = aCN - (aC + b)n \tag{3}$$

The value of j is zero for any equilibrium state. For any nonequilibrium state, the membrane potential is assumed to change at a rate proportional to the surface flux, since the surface flux is directly responsible for changes in the surface or membrane concentration on which the voltage is tacitly assumed to depend.

The voltage is assumed to follow the ratio of the two membrane concentrations occurring at the solution-membrane boundaries with a time constant equal to the electrical time constant of the membrane, which for muscle is of the order of 40 msec. The latter process is more than an order of magnitude faster than the events causing the asymmetry and so does not enter the derivation. The longer times required for a voltage response of the membrane are due to the time necessary to change membrane surface concentrations. These facts may be stated as in Eq. 4, where Q is a constant proportional to the capacity of the surface for ions. The constant Q is evidently proportional to the electrical capacity of the membrane as well.

$$\bar{j} = Q\frac{dV}{dt} \tag{4}$$

A change from state 1 to state 2 is now considered. Using Eqs. 3 and 4, and using the proper value for $n(t)$ given, one obtains

$$(aC'_o + b)\ \Delta n \int e^{-k't}\,dt = Q\int dV \tag{5}$$

recalling that equilibrium values of $\bar{j}$ are all zero. Similarly, considering the change from state 2 back to state 1, one obtains

$$-(a\,C_o + b)\ \Delta n \int e^{-k't}\,dt = Q\int dV \tag{6}$$

If the left-hand sides of Eqs. 5 and 6 are integrated from times zero to in-

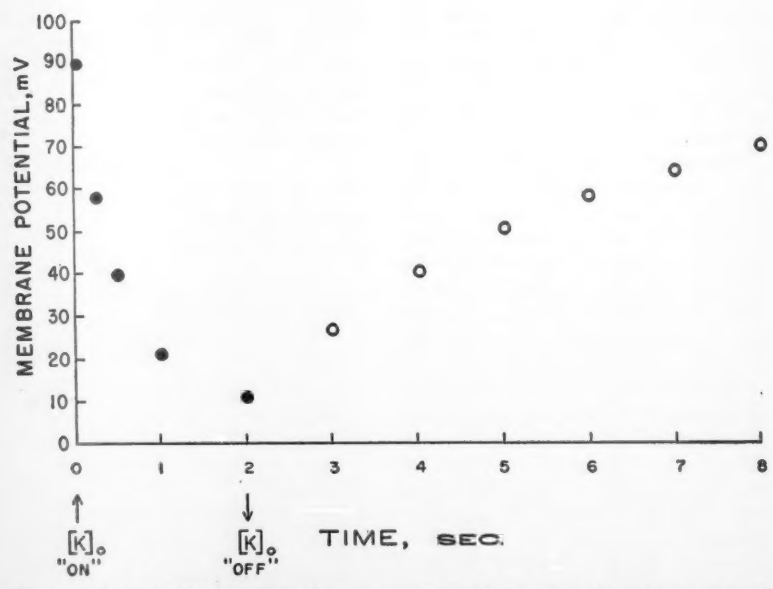

Fig. 1. Depolarization-repolarization sequence plotted for an "adsorption membrane" from Eqs. 8 and 9 and the rate constant values given in the text. The potential at 2.5 mM K is taken as 90 mv (the "resting potential"). The equilibrium depolarization, in 100 mM K, is taken as $\Delta V = -80$ mv. Dots refer to depolarization and open circles to repolarization. The "on" arrow denotes an instantaneous change of concentration to $C'_o = 100$ mM. The "off" arrow denotes an instantaneous change back to the initial concentration $C_o = 2.5$ mM. The sign convention chosen for the potential requires that the constant Q be a negative quantity.

finity, the equilibrium voltages must be obtained upon integration of the right-hand sides. Integration between these limits yields the following relationship for the rate constants:

$$\frac{k}{k'} = \frac{aC'_o + b}{aC_o + b} = \frac{(a/b)\ C'_o + 1}{(a/b)\ C_o + 1} \tag{7}$$

If a value of 0.1 is selected for the constant (a/b), the rate constant for a depolarization as a consequence of changing the potassium concentration from 2.5 to 100 mM will be about 10 times greater than for the subsequent repolarization.

If the integrations of Eqs. 5 and 6 are performed between the limits of time = 0 and time = t, the following time dependence of the voltage is predicted for change 1 to 2 (Eq. 8) and for change 2 to 1 (Eq. 9).

$$V_t = V_1 + \frac{\Delta n(aC'_o + b)}{Qk}(1 - e^{-kt}) \tag{8}$$

$$V_t = V_2 - \frac{\Delta n(aC_o + b)}{Qk'}(1 - e^{-k't}) \tag{9}$$

With $(a/b) = 0.1$ in Eq. 7, a depolarization-repolarization sequence is plotted from Eqs. 8 and 9 when C_o = 2.5 mM and C'_o = 100 mM, k being chosen as 2 sec^{-1} consistent with the half-time of the Hodgkin and Horowicz "on effect." The voltage behavior is similar to that presented by Hodgkin and Horowicz (*1*) for muscle under similar conditions. The value selected for (a/b) is not an unreasonable one since it is of the same order as the value required by Sjodin (*3*) to fit transmembrane flux data (Fig. 1).

It is to be emphasized that the assumption of simple exponential time processes may be regarded as an approximation only. Some quantitative deviations may be expected as a consequence. It has been assumed, for example, that only the external solution is effective in site loading and unloading. The model probably provides a good approximation for the change 1 to 2 in the direction of depolarization. When the outer concentration is changed from a high to a very low value (state 2 to state 1), the approximation may not be as good since the now higher efflux from the cell will become a source of ions for site loading from the inside of the cell. This effect will tend to keep the membrane in the depolarized state and will become less and less a factor as the membrane potential returns to the initial high value. In reality, the driving force for the "off site" movement may vary some while the membrane potential varies, so that the change 2 to 1 cannot be truly exponential as assumed. As this refinement leads to nonintegrable equations, it is not included in the derivation. It is noteworthy, however, that this effect would increase the asymmetry by leading to an even slower "off site" process than calculated. In any event, the source of the time asymmetry is the fact that the processes of site loading and site unloading are different. Site loading is a bimolecular process whereas site unloading is a monomolecular process.

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31 January 1961

Radioprotective Activity of a Phenanthrene Derivative in Mice

Abstract. 2-Acetyl-7-oxo-1,2,3,4,4a,4b,5,6,7,9,10,10a-dodecahydrophenanthrene possessed radioprotective activity when injected subcutaneously (in sesame oil) into 20-day-old male Swiss mice once daily for the 10 days prior to irradiation by cobalt-60 at 30 days of age. Female mice similarly treated were not protected.

Rugh and Wolff (*1*) demonstrated that castration enabled mature male mice to survive whole-body x-irradiation better than intact males. Randall and Selitto (*2*) reported that 2-acetyl-7-oxo-1,2,3,4,4a,4b,5,6,7,9,10,10a-dodecahydrophenanthrene (Ro 2-7239) has antiandrogenic and antimyotrophic activity when administered to testosterone-treated, immature, castrated male rats, while having neither estrogenic nor antiestrogenic activity in female rats. At high doses, Ro 2-7239 also has androgenic activity (*3*). This report considers the radioprotective activity of this phenanthrene derivative in male mice.

The methods used in this study have been previously described (*4*). The mice received 710 r of whole-body Co^{60} irradiation at the rate of 17 to 18 r/min (adjusted to decay of source).

Table 1 gives a summary of five separate experiments, in each of which approximately 12 mice were used at each dose level. Compound Ro 2-7239 both delayed the onset of radiation death and reduced the total mortality, the significance of the protection afforded by the 1000-μg dose at 35 days being $P<0.01$.

Table 1. Protective action of Ro 2-7239 against Co^{60} irradiation when given in daily injections for 10 days before irradiation.

Total dose (μg)	Mice (No.)	Deaths (No.) at specified days after irradiation				
		9	14	21	28	35
0	57	15	39	50	51	51
250	59	7*	29*	38†	41†	42‡
500	57	7	28*	38†	42*	42*
1000	60	9	24†	37†	39†	39†

* $P < 0.05$. † $P < 0.01$. ‡ $P < 0.02$.

Not only did the 1000-μg dose level give optimum protection against radiation death, but it also provided some protection against weight loss due to irradiation. At the observation made 14 days after irradiation, the mean weight of the surviving mice which received 1000 μg of Ro 2-7239 was approximately 2 g (10 percent) greater than the mean weight of the irradiated control mice. An analysis of the variance showed the difference between the means to be statistically insignificant, however. The tendency noted, though, is in contrast to that of the radioprotection elicited by estradiol-17β, in which the mean body weight of the survivors at 15 days after irradiation was essentially the same as that of the irradiated, nontreated survivors (*4*).

Compound Ro 2-7239 elicited no radioprotection whatever when given at the same dose levels to female mice of the same age as the male mice and when given the same dose of irradiation. Approximately 24 mice were used in each of the three treatment groups as well as in the control group. A mortality of 92 to 100 percent was observed for each of the four groups.

These data do not elucidate the mechanism of the radioprotection afforded by Ro 2-7239 (*5*).

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5. Whether this activity is related to its antiandrogenicity is under investigation. The technical assistance of Robert J. Ducios is gratefully acknowledged. This work was supported in part by contract No. AT(30-1)-918 with the U.S. Atomic Energy Commission, and by a grant-in-aid from Hoffmann-La Roche, Inc.

7 February 1961

Optical Properties of Sugar Flavazoles

Abstract. The absorption of glucose flavazole was measured in the ultraviolet and visible regions of the spectrum. Three maxima were observed: 267, 335, and 410 mμ. The absorption at 410 mμ follows Beer's law with 70 percent propanol or water as solvent. The molar absorptivities for glucose, maltose, and lactose flavazoles were the same and equal to 3.7×10^3.

Reducing sugars react with *o*-phenylenediamine and excess phenylhydrazine to produce characteristic derivatives termed flavazoles. The experimental conditions of the reaction have been reviewed, and a number of derivatives have been tabulated (*1*). The reaction is adaptable to oligosaccharides as well as to monosaccharides, although lower yields have been reported (*2*). This is not a serious handicap when paper chromatography is used for purification. A series of starch dextrins from four to eight glucose units were readily separated and purified by this method, thus permitting their preparation on a semimicro scale.

The flavazoles are bright yellow and can be estimated by colorimety. The spectrum through the ultraviolet and visible ranges was measured for glucose flavazole. The intensity of the absorption taken at 410 mμ is proportional to concentration within the limits of experimental error. Furthermore, the chromophoric group does not appear to be influenced by substitution at positions 4 or 6 with other hexose units. The molar absorptivity at 410 mμ for glucose, maltose, and lactose flavazoles was found to be the same within experimental error (2 to 3 percent).

Glucose, maltose, and lactose flavazoles were prepared by the conventional procedure (*2*). Four crystallizations were usually adequate to remove all traces of impurities as revealed by paper chromatography. Paper chromatography is a much more sensitive method for detecting impurities than is the melting point. This is particularly true of the oligosaccharides. The solvent system, six parts 1-butanol, four parts pyridine, and three parts water, used frequently for carbohydrates was used. The derivatives after crystallization were dried in a vacuum oven for 6 hr at 50°C and stored over calcium chloride. The absorbancies were read in 70 percent propanol (Eastman-redistilled) against a solvent blank in each case.

A Beckman model DU spectrophotometer was used for the absorption studies, and 1-cm quartz cells were used in the ultraviolet as well as in the visible spectrum.

Two absorption peaks, 267 and 335 mμ, were found in the ultraviolet, and one, 410 mμ, was found in the visible spectrum (Fig. 1). The latter was selected for quantitative studies because it is in the visible range and therefore can be used with a simple colorimeter. It should be noted, however, that the absorption in the ultraviolet is much more intense than it is in the visible. Molar absorptivities were as follows: at 267 mμ, 3.98×10^4; at 335 mμ, 1.01×10^4; at 410 mμ, 3.7×10^3.

A slight solvent effect could be observed. When distilled water was used as solvent in place of 70 percent propanol, the peak in the visible was shifted to 405 mμ. The height of the peak, however, was not significantly changed.

The absorption obeyed Beer's law very well over the workable range of the Beckman instrument. An exact correspondence between glucose, maltose, and lactose flavazoles could be observed when the absorbancy readings were plotted against the molar concentration (the molecular weight of glucose flavazole is 336 and of maltose and lactose flavazole, 498). An equally good check was obtained when water was used as solvent, and the absorbance was measured at 405 mμ instead of at 410 mμ. Since mono- and disaccharide flavazoles are only sparingly soluble in water but appreciably soluble in 70 percent propanol, the latter solvent is preferable.

It has been pointed out in a previous communication (*3*) that paper chromatography of flavazoles could be used to advantage in determining the structure of oligosaccharides. Acidic or enzymic hydrolysis of an oligosaccharide flavazole yielded a number of fragments consisting of reducing sugars and flavazoles of a lower degree of polymerization. These could be separated by paper chromatography and subsequently identified, permitting a formulation of the original oligosaccharide. It would be of advantage if such qualitative observations could be combined with quantitative estimations. A number of methods are currently available for estimating carbohydrates separated by chromatography (*4*). Glucose and maltose flavazole fragments can be easily eluted from paper chromatograms and determined

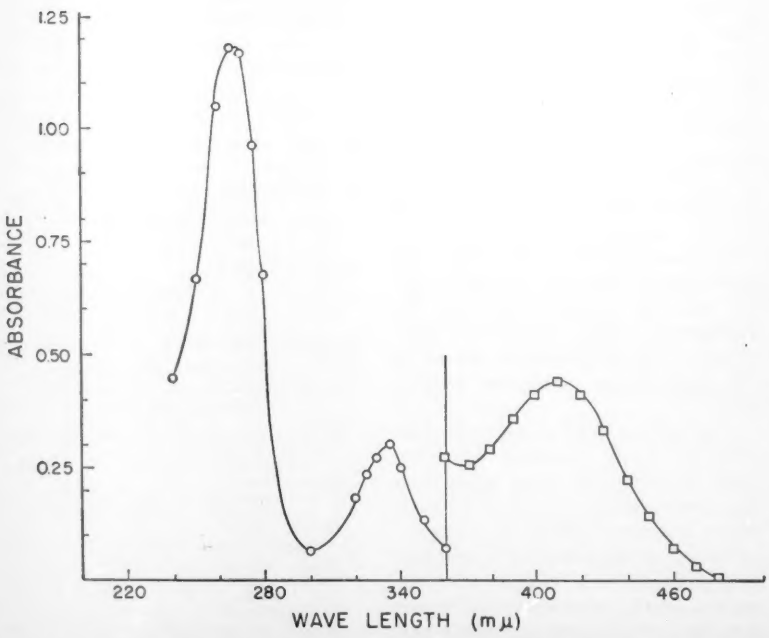

Fig. 1. Absorption spectrum of glucose flavazole in 70 percent 1-propanol. Circles indicate the ultraviolet (0.001 percent) and squares the visible (0.004 percent).

quantitatively by the method described above. For a usual Beckman cell an amount readily obtained from a chromatographic strip (0.25 to 0.50 mg) is adequate for a reliable determination (*5*).

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28 February 1961

Deamination of Adenine by Ionizing Radiation

Abstract. A small amount of hypoxanthine is formed when a solution of adenine is irradiated. This has been detected by using C^{14}-labeled adenine and the techniques of paper chromatography and liquid-scintillation counting. The biological significance of this conversion is suggested.

Deamination takes place quite readily when an aminopurine or aminopyrimidine is hydrolyzed with acid (*1*). Ten-percent hydrochloric acid converts cytosine into uracil (*2*). Nitrous acid deaminates adenosine to inosine (*3*) and guanosine to xanthosine (*4*). A similar conversion takes place enzymatically. Intestinal deaminases, for example, convert adenine to hypoxanthine, adenosine to inosine, and adenylic acid to inosinic acid (*5*). The ultraviolet irradiation of adenine solutions has been reported to give trace quantities of hypoxanthine (*6*).

Previous workers had concluded that deamination of this type probably did not take place under the influence of ionizing radiation (*7*). In our studies of the radiation decomposition of nucleotides and related compounds, however, we have found that adenine is converted into hypoxanthine. The yield is small, but significant.

About 250 μl of a 0.1 percent solution of adenine-2-C^{14} (specific activity, 1.3 mc/mmole) were sealed in a vacuum (*8*). To expel any dissolved oxygen, a steady stream of N_2 was bubbled through the solution for about 10 min before the sample was sealed.

A 1.5 kc cobalt-60 source was used for the irradiation. The dosage was calculated by means of the Fricke ferrous sulfate dosimeter. The radiation intensity was 5×10^6 rad/hr.

The irradiation products were analyzed by paper chromatography, with Whatman No. 4 paper and propanol–ammonia–water and butanol–propionic acid–water as solvents (*9*). Twenty-five microliters of the irradiated solutions of adenine were spotted on paper together with 10 μl of 0.1 percent inactive hypoxanthine as carrier. The ultraviolet-absorbing areas were carefully marked out. Autoradiography with x-ray films showed darkening of the film corresponding to the hypoxanthine spot. The radioactivity could have come only from the adenine, showing the conversion of adenine to hypoxanthine. The chromatography of the control was done at the same time as that of the irradiated samples. Thus, bacterial deamination could have been, at most, a minor effect.

In one experiment, the hypoxanthine spot was eluted with 0.1 percent formic acid and rechromatographed with fresh carrier hypoxanthine, with butanol–water (*10*) and isobutyric acid–ammonia–ethylene diaminetetraacetic acid (*11*) as solvents. The radioactivity was concentrated on the hypoxanthine spot, which confirmed the formation of radioactive hypoxanthine.

The hypoxanthine spots were eluted with 0.1 percent formic acid and counted with a liquid scintillator having an internal standard of C^{14}-labeled toluene. The same technique was used for the estimation of residual adenine. The results of the experiments are shown in Table 1.

The biological importance of a deamination of this type may be very great. If it would be legitimate to extrapolate from a high dose level to a low dose level, we may have a possible clue to the origin of a radiation mutation. When the ribonucleic acid of tobacco mosaic virus was heated with HNO_2, the amino bases were converted to the hydroxy bases without splitting of the nucleotide chain. Deamination of a large number of nucleotides resulted in the inactivation of the molecule (*12*). More gentle treatment by controlled action of HNO_2 gave a maximum number of mutations when an average of 1 deamination resulted per 6000 nucleotides (*13*).

Table 1. Formation of hypoxanthine from adenine by ionizing radiation. In all experiments the initial activity was 4.1×10^5 disintegrations per minute (dpm).

Expt.	Dose (10^6 rad)	Residual adenine (%)	Hypoxanthine	
			Act. (dpm)	Amt. (%)
Control	0	100	330	0.08
1	1	87.7	3602	0.88
2	2	75.4	3807	0.98
3	5	60.1	7840	1.9
4	10	44.4	3839	0.9

Because hypoxanthine, xanthine, and uracil normally exist in the keto form (*14*), the deamination of adenine to hypoxanthine will result in the disruption of the hydrogen bonding between adenine and thymine, suggested by the Watson and Crick structure of deoxyribonucleic acid (*15*). From theoretical considerations Lavalle (*16*) has pointed out that deamination of adenine would result in the replacement of an adenine-thymine base pair by a guanine-cytosine pair, altering the molecular code of heredity (*17*).

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* Present address: Miller Institute for Basic Science, University of California, Berkeley (1960–61).

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12–19. Fast Reactions, summer school, Cambridge, England. (Secretary of the Summer School, Dept. of Physical Chemistry, Lensfield Road, Cambridge)

13–18. Microchemical Techniques, intern. symp., University Park, Pa. (H. J. Francis, Jr., Pennsalt Chemical Corp., P.O. Box 4388, Chestnut Hill Post Office, Philadelphia 18, Pa.)

13–18. Theoretical Aspects of Magnetohydrodynamics, seminar, University Park, Pa. (Conference Center, Pennsylvania State Univ., University Park)

13–19. International Assoc. of Applied Psychology, 14th congr., Copenhagen, Denmark. (Congress Secretariat, 19 Sankt Pederstraede, Copenhagen K.)

13–19. Training for Research in the Processes of Vision, 1st intern. conf., Rochester, N.Y. (Office of Public Information, River Campus Station, Rochester)

14–17. Calorimetry Conf., intern., Ottawa, Canada. (J. E. Kunzler, Bell Telephone Laboratories, Murray Hill, N.J.)

14–19. International Medical Conf. on Mental Retardation, 2nd, Vienna, Austria. (Miss E. Langer, Div. of Maternal and Child Health, State House, Augusta, Maine)

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21–2. International Congr. of Practical Medicine, Merano, Italy. (Bundesärztekammer, 1 Hädenkampfstrasse, Cologne, Germany)

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22–30. International Conf. on Protozoology, Prague, Czechoslovakia. (N. D. Levine, College of Veterinary Medicine, Univ. of Illinois, Urbana)

23–25. Gas Dynamics, symp., biennial, Evanston, Ill. (J. J. Harford, American Rocket Soc., 500 Fifth Ave., New York, N.Y.)

23–26. Electron Microscope Soc. of America, Pittsburgh, Pa. (Miss M. L. Rollins, Agricultural Research Service, U.S. Department of Agriculture, P.O. Box 19,687, New Orleans 19, La.)

23–26. Institute of Management Sciences, 8th annual intern., Brussels, Belgium. (W. Smith, Inst. of Science and Technology, Univ. of Michigan, Ann Arbor)

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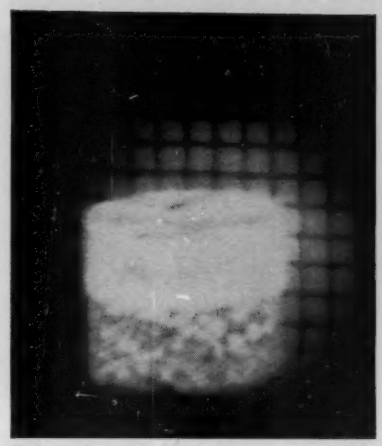

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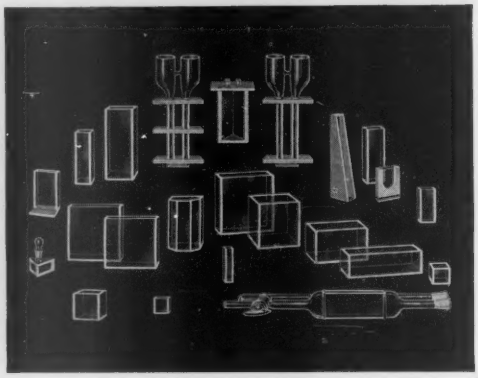

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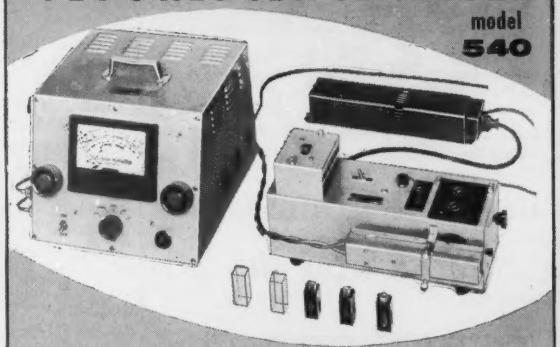

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Association of Midwest College Biology Teachers (J. D. Novak, Dept. of Biological Sciences, Purdue Univ.)

Biometric Society (ENAR) (H. E. McKean, Statistical and Computing Laboratory, Purdue Univ.)

Botanical Soc. of America (A. C. Leopold, Dept. of Horticulture, Purdue Univ.)

Entomological Soc. of America (Section A) (L. Chandler, Dept. of Entomology, Purdue Univ.)

Genetics Soc. of America (A. B. Burdick, Dept. of Biological Sciences, Purdue Univ.)

Mycological Soc. of America (J. S. Lovett, Dept. of Biological Sciences, Purdue Univ.)

National Assoc. of Biology Teachers (J. D. Novak, Dept. of Biological Sciences, Purdue Univ.)

Nature Conservancy (A. A. Lindsey, Dept. of Biological Sciences, Purdue Univ.)

Phycological Soc. of America (A. T. Guard, Dept. of Biological Sciences, Purdue Univ.)

Sigma Delta Epsilon (Miss V. B. White, Dept. of Foods and Nutrition, Purdue Univ.)

Society for Industrial Microbiology (W. N. Cannon, Lilly Research Labs., Eli Lilly and Co., Indianapolis, Ind.)

Society for the Study of Development and Growth (F. H. Wilt, Dept. of Biological Sciences, Purdue Univ.)

Society for the Study of Evolution (L. Chandler, Dept. of Entomology, Purdue Univ.)

Tomato Genetics Cooperative (A. B. Burdick, Dept. of Biological Sciences, Purdue Univ.)

Wildlife Disease Assoc. (S. M. Gaafar, Dept. of Veterinary Microbiology, Pathology and Public Health, Purdue Univ.)

27–1. Coordination Chemistry, 6th intern. conf., Detroit, Mich. (S. Kirschner, Dept. of Chemistry, Wayne State Univ., Detroit 2)

28–30. Mathematical Assoc. of America, Stillwater, Okla. (H. L. Alder, MAA, Univ. of California, Davis)

(See issue of 16 June for comprehensive list)

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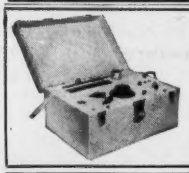

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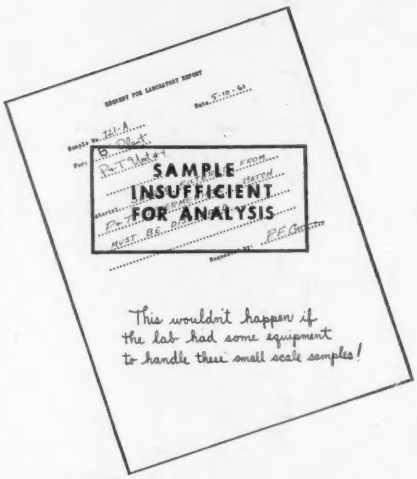
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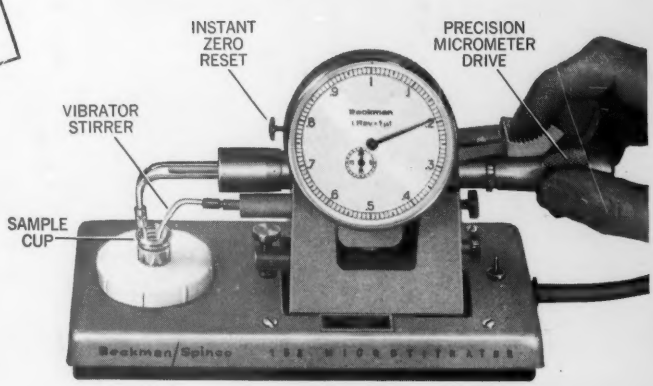

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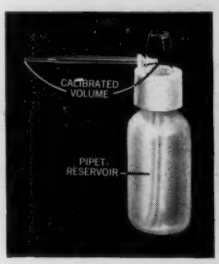

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